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A CRITICAL REVIEW OF THE EPIDEMIOLOGY OF HUMAN TRYPANOSOMIASIS IN AFRICA

By

M. T. ASHCROFT, M.A., B.M., B.CH., D.P.H., D.T.M. & H.

Recently of the East African Trypanosomiasis Research Organization

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The epidemiology of sleeping sickness is somewhat confused when compared with that of some other insect-borne diseases such as yellow fever, plague or malaria. This review attempts to point out the factors which are responsible for the confusion and tries to clarify our present knowledge in the light of recent developments.

The discovery of Trypanosoma brucei, T. gambiense and T. rhodesiense

An understanding of the epidemiology of human trypanosomiasis in Africa is dependent on an understanding of the relationship between *Trypanosoma brucei*, *T. gambiense* and *T. rhodesiense*. The discovery of these parasites is briefly described in order that subsequent work on their relationship can be fully appreciated.

A tsetse-borne trypanosome was first found in 1895 by BRUCE in wild and domestic animals in Zululand; it was sent to England and described by KANTHACK, DURHAM and BLANDFORD (1898) and named *T. brucei* by PLIMMER and BRADFORD (1899).

Trypanosomes were not known to infect man until they were detected in the blood of the captain of a steamboat on the River Gambia by FORDE; they were described by DUTTON (1902) and named *T. gambiense*. Because the patient had few symptoms except fever, *T. gambiense* was regarded as the causative agent of what was called trypanosomal fever and its connexion with sleeping sickness, a disease which had been recognized clinically for many years, was not known. In 1903, however, CASTELLANI and BRUCE and NABARRO, leading the Sleeping Sickness Commission of the Royal Society in Uganda, discovered that the trypanosomes were the causal organisms of sleeping sickness and it was shown that the vector of the disease was the tsetse fly, *Glossina palpalis*.

The position remained relatively simple—one tsetse-borne trypanosome *T. gambiense*, infecting man, and others, including *T. brucei*, infecting animals —until STEPHENS and FANTHAM (1912) described a polymorphic trypanosome, *T. rhodesiense*, found in a patient in Rhodesia, which they differentiated from *T. gambiense*, which was also polymorphic, because trypanosomes with nuclei in the posterior portion of their bodies (the so-called posteronuclear forms) were seen in blood of infected laboratory animals; the trypanosome was also shown to be more virulent than *T. gambiense* to all animals, including man.

Another development heralded a problem—the relationship between *T. brucei* and *T. rhodesiense*—which soon became the subject of a great deal of controversy. KINGHORN and YORKE (1913) studied various aspects of trypanosomiasis for the British South Africa Company in Rhodesia, and in a report on their findings of the incidence of trypanosomiasis in game they stated that 16% of the animals examined were infected with *T. rhodesiense*. It was soon pointed out that they had omitted to recognize the possibility that some of the parasites might have been *T. brucei*. BRUCE *et al.* (1914), surprised at this apparent absence of *T. brucei*, examined trypanosomes from animals infected with a strain which was presumed to be *T. brucei* because it had been isolated in Zululand, whence Bruce had obtained his original strain; the trypanosomes were found to be identical with parasites isolated from man in Rhodesia. Bruce *et al.* also pointed out that the trypanosomes were originally described by Bruce in his paper of 1895 as haematozoa which vary among themselves a good deal in size and shape, and that figures in this paper showed a distinct dimorphic trypanosome. KANTHACK, DURHAM and BLANDFORD (1898) in their description of Bruce's trypanosome had stated "the Nagana parasites vary considerably both in size and form; they may be long and pointed or blunt-ended and somewhat stouter". There could be no doubt that the trypanosomes in man and in the wild animals were identical in morphology. PLIMMER and BRADFORD (1899), however, had not described the polymorphism of *T. brucei* and it is probable that the morphology had changed during the maintenance of the strain in laboratory animals—a process which we now know occurs readily. Indeed, LAVERAN and MESNIL (1907) classified *T. brucei* as a monomorphic trypanosome. In view of these circumstances it is not surprising that Kinghorn and Yorke had not recognized that their trypanosomes were similar to *T. brucei*.

Once this initial difficulty had been surmounted and the morphological identity of the animal and human trypanosomes had been appreciated, the vital problem of their relationship arose.

The relationship between T. brucei and T. rhodesiense

BRUCE *et al.* (1914) studied several strains of polymorphic trypanosomes obtained from wild animals and from patients suffering from sleeping sickness in Nyasaland and Rhodesia. They found such striking morphological and physiological similarities in all the strains (findings which have been confirmed many times) that they concluded that the evidence was in favour of *T. rhodesiense* and *T. brucei* being one and the same parasite, a conclusion which YORKE and BLACKLOCK (1914) also reached. Bruce *et al.* were aware, however, that the trypanosomes might differ in their infectivity to man, and as at that time because of the lack of an adequate cure, man could not be infected experimentally, they suggested that their relationship would be elucidated by the distribution of sleeping sickness; their actual words were "if *T. brucei* and *T. rhodesiense* are identical we must expect to find cases of 'Nyasaland sleeping sickness' cropping up in all parts of Africa where *G. morsitans* and *T. brucei* exist". Bruce *et al.* thought that this distribution would be found to occur because sporadic cases of sleeping sickness were, at the time they were writing, being diagnosed in widely separated areas of Rhodesia.

In contrast, KLEINE and ECKARD (1913) and KLEINE (1914, 1923, 1928) who were working in Tanganyika were quite certain that the distributions of the animal and human trypanosomes were not the same. They pointed out that the caravan road from Tabora to Ujiji passed for a long distance through an area infested with *G. morsitans* and along this road had passed many German officials and Africans, none of whom had been infected although the route was fatal to domestic animals some of which succumbed to *T. brucei*. The railway from Tabora to Kigoma passed through this fly-belt and was completed in 1914; despite the close watch kept by the medical authorities who were well aware of the menace of sleeping sickness, no cases of the disease were diagnosed (*T. rhodesiense* was first found in this area about 1926 and FAIRBAIRN (1948) showed it had been introduced from the south). It is now known for certain that there are areas in which tsetse flies and *T. brucei* exist but in which sleeping sickness in man, despite his contact with the fly, is not present; Zululand is an obvious example.

TAUTE (1913) was so convinced that the human and animal trypanosomes were not identical that he bravely inoculated himself with animal blood containing polymorphic trypanosomes and allowed himself to be bitten by infected tsetse flies; he was not infected. TAUTE and HUBER (1919) inoculated 6 strains obtained from naturally infected horses and mules into 129 men in Tanganyika; none was infected.

Despite these two lines of evidence against the identity of the trypanosomes of man and animals, there was a considerable body of opinion (YORKE, 1920; DUKE, 1915, 1921) which was reluctant to accept that the pathogenicity to man is a stable difference between *T. brucei* and *T. rhodesiense*. The non-pathogenicity to man of the strains tested by TAUTE (1913) and TAUTE and HUBER (1919) was explained by assuming that man was, on the whole, resistant to *T. brucei* and that only the exceptional person could be infected;

later it will be shown that this explanation has not been confirmed by experiments. The differences in the distributions of *T. brucei* and *T. rhodesiense* could not be accounted for satisfactorily.

Renewed interest was taken in the controversy in 1930. YORKE, ADAMS and MURGATROYD (1930) demonstrated that human serum has a trypanolytic action *in vitro* at 37°C. on strains of *T. equiperdum*, *T. congolense* and *T. rhodesiense* which had been syringe-passaged for some years, but less so on a recently isolated strain of *T. rhodesiense* and not at all on an old strain of *T. gambiense*. This discovery was of considerable interest because, although LAVERAN (1902, 1904) had shown that normal human serum inhibited the course of *T. brucei* but not *T. gambiense* infections when inoculated into infected mice, *i.e. in vivo*, no action had been demonstrated *in vitro*. A great many investigations, which have been reviewed by YORKE, ADAMS and MURGATROYD (1930) and by CULBERTSON (1935), have been made on the *in vivo* trypanocidal effect, which has been shown to be due to a factor in the globulin fraction of the serum proteins which is diminished in certain diseases, especially in those involving the liver. On the basis of both this *in vivo* and their own *in vitro* work, YORKE, ADAMS and MURGATROYD (1930) suggested that *T. brucei* is synonymous with *T. rhodesiense* but that normal human beings cannot be infected by the parasite derived from game because of the trypanocidal power of human blood. However, in persons suffering from certain diseases or with improper diet the trypanocidal power of the blood would be lost and consequently such persons could be infected. Once established in man the parasites would become serum-resistant and could then be transmitted through healthy men, but if passed on to animals they would lose their serum-resistance (as had the syringe-passaged strain of *T. rhodesiense*) and hence their infectivity to man. In contrast to *T. rhodesiense*, *T. gambiense* is well adapted to man and is more tenacious in retaining its resistance to human serum and its infectivity to man.

Their hypothesis makes the doubtful assumption that the resistance of the parasite to human serum is the basic factor which governs its infectivity to man. However, bacteriologists do not regard experiments with serum *in vitro* as sufficient to explain the presence or absence of immunity to infection with bacteria; for example, the serum of the rabbit is actively bactericidal toward *Bacillus anthracis*, yet that animal is very susceptible to experimental infection. Experiments have shown that in this connexion what is true in bacteriology is also true in protozoology. COLLIER (1924) and LESTER (1933) made strains of *T. brucei* resistant to human serum *in vivo* and inoculated large doses of these strains into men without producing any infection. FAIRBAIRN (1933) infected himself with a strain of *T. rhodesiense* which had been passed through rats until it was sensitive to his own serum *in vitro*.

Another test of the hypothesis was to pass strains of *T. rhodesiense* through animals and to see if the infectivity of the strain to man was lost as had been postulated. Such an experiment became possible because of the introduction of Antrypol which cures early *T. rhodesiense* infections and therefore enables volunteers to be infected with safety. CORSON (1932) syringe-passaged a strain taken from a patient through sheep and goats for 19 months and then infected himself by the inoculation of rat blood. FAIRBAIRN (1933) syringe-passaged a strain from a patient through rats for 11 months and then infected himself by the inoculation of rat blood. CORSON (1935) transmitted a strain

from a patient through several dikdiks by *G. morsitans*; after one year of transmission a fly fed on and infected a man. CORSON (1936a, 1937a, 1937c, 1938a, 1938b, 1939a, 1939c), FAIRBAIRN and BURTT (1946), WILLETT and FAIRBAIRN (1955) and ASHCROFT (1959a) have recorded the transmission of a strain of *T. rhodesiense* through *G. morsitans* and sheep for 23 years; lines of the strain were also transmitted through monkeys for 10 years and through various species of antelope for 6 years; men could be infected throughout the experiment by the bites of infected flies or by the inoculation of infected rat blood. Some men were not infected by the bite of an infected fly and FAIRBAIRN and BURTT (1946) showed that this was due to the fact that some flies may inoculate too few trypanosomes and was not due to loss of infectivity of the strain. This finding accounts for the apparent changes in infectivity to man—deduced by the results of fly bite—of several strains of *T. rhodesiense* transmitted by DUKE (1933, 1935a, 1935b, 1937a) through *G. palpalis* and a variety of animals and which led him to conclude that the infectivity to man is a labile property and not a stable distinction between *T. brucei* and *T. rhodesiense*. A strain of *T. rhodesiense* has been cyclically passaged through guineapigs for 14 months and a man was infected by the inoculation of rat blood (EATRO, 1958).

These experiments show that the pathogenicity to man is not lost during passage through animals. One exception must, however, be mentioned; FAIRBAIRN (1956) and ASHCROFT (in preparation) showed that a strain of *T. rhodesiense* which had been syringe-passaged for many years through rats and mice had lost its power to infect man; the strain had, however, changed considerably in many other ways.

Experiments have shown that strains of *T. brucei* are consistently non-pathogenic to man. LESTER (1933), in Nigeria, inoculated 43 men with one strain of *T. brucei* without producing any infection. FAIRBAIRN and CULWICK (1949) inoculated 10 men with blood from rats infected with a strain of *T. brucei* and fed flies infected with the same strain on 39 men without any resulting infection. Reference has already been made to the experiments of TAUTE (1913), TAUTE and HUBER (1919) and COLLIER (1924). VAN HOOF (1947), however, briefly recorded a transitory symptomless infection in 1 of 7 volunteers bitten by *G. palpalis* infected with *T. brucei*; one would like fuller documentation of this unique finding.

It is difficult to reconcile these experiments with the possibility that *T. brucei* and *T. rhodesiense* are synonymous and that only the exceptional human being can be infected; in contrast, the bulk of the evidence, both epidemiological and experimental, shows that the trypanosomes are distinct and that *T. rhodesiense* is consistently infective to all human beings and that *T. brucei* is consistently non-infective.

The role of wild animals in the epidemiology of T. rhodesiense sleeping sickness

If *T. brucei* and *T. rhodesiense* were identical it is obvious that wild animals which are frequently infected with *T. brucei* would have played a large part in the epidemiology of the human disease, but as they appear to be distinct, the role of animals must be considered separately.

Numerous animals have been experimentally infected with *T. rhodesiense*.

ASHCROFT, BURTT and FAIRBAIRN (1959) reviewed this work and classified African wild animals into various groups according to their reactions to infection; they suggested that this classification would be also valid for reactions to *T. brucei* infections because the course of *T. brucei* and *T. rhodesiense* infections were similar in animals of the same species. One group, which includes Thomson's gazelles, dikdiks, jackals and monkeys, was killed by the infection; bushpigs and warthogs could be infected with difficulty but the parasitaemia was light and did not persist long; in some species, among which were reedbucks and bushbucks, the infection was relatively heavy and persisted for some time before recovery. Recently the work of WEITZ and JACKSON (1955), WEITZ and GLASGOW (1956) and GLASGOW, ISHERWOOD, LEE-JONES and WEITZ (1958), based on refinements in serological techniques for the identification of blood meals of arthropods, has shown that some of these animals may be important hosts of *G. morsitans*, *G. swynnertoni* and *G. pallidipes*, which are the vectors of *T. rhodesiense*, so the results are strong presumptive evidence for the existence of an animal reservoir of *T. rhodesiense*.

Few attempts, which require the use of volunteers in order to distinguish *T. brucei* from *T. rhodesiense*, have been made to prove the existence of *T. rhodesiense* in wild animals. ASHCROFT (1958) isolated one strain of polymorphic trypanosomes, which proved to be *T. brucei*, from 74 animals of various species shot in two areas of Tanganyika where *T. rhodesiense* sleeping sickness is endemic. Recently, however, HEISCH, MCMAHON and MANSON-BAHR (1958) succeeded in isolating *T. rhodesiense* from a bushbuck in a *G. pallidipes* area in Kenya.

T. rhodesiense has been isolated on 3 occasions from wild *G. pallidipes* as reported by MCKICHAN (1944) and by EATRO (1956, 1958). As *G. pallidipes* is primarily a zoophilic tsetse fly it seems probable that these infections had been acquired from wild animals.

Although the experimental infection of the animal hosts of tsetse flies with *T. rhodesiense* and the detection of the trypanosome in *G. pallidipes* and in a bushbuck leave no doubt that animals in the vicinity of human *T. rhodesiense* infections are sometimes infected, it is only by epidemiological studies that the *importance* of the part played by animals in the transmission of human disease can be estimated. It must be recognized, however, that there are difficulties involved in such studies which make it almost impossible to draw incontrovertible conclusions. Sleeping sickness due to *T. rhodesiense* is often contracted in remote areas. It may be impossible to discover where exactly the disease was contracted, not only because the patients may have been wandering through the bush in search of fish or honey or hunting but also because of difficulty in extracting reliable information. The disease may be difficult to diagnose and it is not easy to assess the importance of chronic infections, relapses following treatment, and " carriers ", as sources of infection for the fly.

ROSS and BLAIR (1956) have reviewed the cases of " carriers " in Rhodesia; some of these patients have been observed for several months with trypanosomes in the blood but have been entirely without symptoms; Ross and Blair suggested that such persons might be responsible for the persistence of *T. rhodesiense* in Rhodesia. DYE (1927) observed one patient in Tanganyika who had trypanosomes in the blood for one month but was

completely free from symptoms. ROBERTSON (personal communication) has also seen an infected person who remained apparently healthy for 2 months in Busoga, Uganda. On the other hand, LAUFER (1955) examined blood slides from about 9,000 persons in a part of Kibondo District, Tanganyika, where an outbreak of sleeping sickness was occurring; not a single symptomless carrier was found. ROBERTSON (personal communication) examined blood slides from 2,400 people in an endemic area of Busoga, Uganda, and found trypanosomes in one man only and he had been previously treated and was in relapse. On the whole it seems that the majority of persons suffering from sleeping sickness due to *T. rhodesiense* are so ill that they could not have much contact with the tsetse fly, or if they do, for a limited period only; symptomless carriers are unusual.

Another factor is the long length of life of the insect vector; some tsetse flies, but probably very few, may live as long as six months (see BUXTON, 1955). It is therefore possible that a single infected man wandering through the bush far from human habitation might be responsible for the infection of a similar wanderer 6 months later. It might appear to an investigator, however, that animals must have been acting as a reservoir. Conversely, if persons living in proximity become infected it has sometimes been erroneously concluded that the evidence suggests that trypanosomes had passed from man to man; it is just as likely, however, that the movements of such persons were similar and that they all had been bitten by tsetse flies which had acquired their infections from animals.

SWYNNERTON (1923, 1925) investigated an outbreak of *T. rhodesiense* sleeping sickness in Maswa District, Tanganyika. He observed very little game but many tsetse flies and he therefore maintained that the transmission must be from man to man. It is, however, difficult to accept the absence of wild animals if the tsetse fly responsible for this epidemic, *G. swynnertoni*, was abundant. It has been generally found that the closely related tsetse fly, *G. morsitans*, is unable to exist on man or his domestic animals (see BUXTON, 1955); it is possible that the *G. swynnertoni* in Maswa were feeding on unobtrusive or relatively small game such as bushpig or bushbuck. DUKE (1923) investigated the same outbreak. He also was struck by the abundance of tsetse flies and he traced most cases to previous human contacts; indeed, he was so impressed by the chances of contact that he suggested that the transmission was mechanical—that is by the transference of blood from an infected to a healthy man by the proboscis of the tsetse fly without cyclical development taking place—an opinion which he later abandoned. DAVEY (1924, 1925), visiting Maswa some months after Swynnerton and Duke, saw plenty of game and found cases of the disease which he could not trace to previous human contact; he concluded that the evidence from the outbreak was compatible with the view that *brucei* and *rhodesiense* were identical and that game, as a carrier of *T. brucei*, was important as a reservoir. These three investigations of the same outbreak demonstrate the difficulties involved in the study of the epidemiology of disease due to *T. rhodesiense*; the data collected were not exact enough to justify the contradictory conclusions which were reached.

KINGHORN (1925) studied the incidence of *T. rhodesiense* sleeping sickness in the Luangwa valley of Northern Rhodesia; he believed that the game must have been acting as a reservoir because the human cases occurred so

sporadically and far apart. He suggested that the exacerbations, which sometimes occurred, of the endemic incidence of trypanosomiasis, were largely due to a superimposition of a man-fly-man cycle of transmission on the more usual game-fly-man transmission. MACLEAN (1926) studied the spread of sleeping sickness in the Ufipa District of Tanganyika and concluded that it was carried from village to village by the movements of infected persons. DYE (1927) investigated a small outbreak in the Southern Province of Tanganyika; he found a greater incidence of trypanosomiasis in villages infested with tsetse flies than in those surrounded by clearing. All the inhabitants of one badly affected village were evacuated for two months and then allowed to return and observed for two months; no further cases of sleeping sickness were diagnosed. He concluded therefore that there was no evidence that the spread of the disease was anything but from man to man, but it is possible that his observation period was insufficiently long.

ROBERTSON and BAKER (1958) studied an outbreak of *T. rhodesiense* sleeping sickness in Busoga, Uganda, and suggested that the transmission of the disease was from man to man. This opinion was mainly based on the distribution of the cases in two main foci in the tsetse fly infested area. The present author visited parts of the area in 1958 and observed that not only were the cases concentrated in these two foci but so was the population; large areas of forest are uninhabited and probably visited very seldom. In such circumstances a focal distribution of the disease would be expected whether the animals were acting as a reservoir or whether the disease was limited to man. On Sigulu Island, one of the foci of the infection, recent immigrants to the island had tilled the land right up to the margins of the forest in which *G. pallidipes* were numerous; they complained bitterly about the depredations of waterbuck and it seems likely that the animals might have been acting as a reservoir.

FAIRBAIRN (1948) studied the spread of *T. rhodesiense* sleeping sickness through Tanganyika and concluded that epidemics were started in new areas by the arrival of infected persons and that, once the disease had been introduced into an area, the game became infected and acted as a reservoir. The distribution and pattern of sleeping sickness in Tanganyika certainly indicate that infection of animals does play some part. Two examples follow.

The River Ugala area in Tabora District was depopulated because of sleeping sickness in 1925–26. In this region there is said to be hardly a man present during the 6 months of the rainy season but, regularly, when men return in the dry season to fish or to collect honey, some contract sleeping sickness, a feature which suggests that the trypanosome is maintained during the rainy season in the game. The River Ugala is part of the Malagarasi River system which drains much of the Western Province into Lake Tanganyika. The surrounding area is extremely sparsely populated but game and *G. morsitans* are abundant and in it over half the cases of *T. rhodesiense* sleeping sickness diagnosed in all Africa in 1953, 1954 and 1955 were contracted. The incidence of sleeping sickness in the Western Province, in which the area mainly lies, for these three years was 538, 895 and 636 cases respectively (APTED, 1956). This prevalence of the disease in a locality which is so sparsely inhabited suggests the existence of an animal reservoir. JACKSON (1955) reported 25 cases of sleeping sickness contracted by his staff in remote and little visited camps situated in this area. Jackson, who possessed unrivalled knowledge of the population and life history of *G. morsitans*, concluded that the chances of his

men having acquired their infection from other infected men were very small indeed. Another area where the game appears to be acting as a reservoir is around Magugu, 85 miles S.W. of Arusha. The disease was first diagnosed in this region in 1944; in the first three years of the epidemic 458 cases in all were found but the numbers have diminished and in 1953, 1954 and 1955 respectively, 50, 41 and 32 cases were diagnosed (APTED, 1956). It is difficult to explain the continuing low endemicity by man-fly-man spread because periods of some months occur in which no new cases are diagnosed. JACKSON (1955) described how one of his fly boys was infected at Daga-Iloi in this area; there was neither settlement in, nor right of way through, Daga-Iloi and circumstances showed that the man must have been infected within one mile from Jackson's headquarters where, despite constant surveillance, no other cases had been diagnosed; he therefore thought it unlikely that the tsetse fly, which had bitten the fly boy, had acquired its infection from another human being.

For reasons already advanced, incontrovertible conclusions can be reached only with extreme difficulty from any one of the studies of the epidemiology; taken as a whole, however, the evidence does suggest that wild animals must play a role in some areas but that man-fly-man transmission may also be important.

One difficulty in understanding the part played by an animal reservoir is the localized distribution of human *T. rhodesiense* infection; adjacent to where the disease occurs are areas inhabited by tsetse flies and wild animals and visited by man but in which the disease does not occur. This can be seen by the comparison of a map showing the areas where *T. rhodesiense* sleeping sickness is endemic in Tanganyika (APTED, 1956) with a map of the tsetse fly distribution. If *T. rhodesiense* and *T. brucei* infections of animals are similar —as all experiments show—it might be expected that the distribution of both trypanosomes would be the same. CULWICK, FAIRBAIRN and CULWICK (1951) suggested that hybridization between *T. brucei* and *T. rhodesiense* takes place and the infectivity of *T. rhodesiense* might be lost in such a process; they based this theory on the measurement of the slender forms of strains of *T. brucei* and of *T. rhodesiense* in single and mixed infections in rats; they found that the mean lengths of the slender forms of the mixed strains were significantly different from those of the parent strains. This evidence cannot be accepted, however, unless it is possible to differentiate exactly between slender and other forms of the polymorphic trypanosomes (a controversial subject) because, if not, it would be impossible to obtain valid measurements of the mean length of slender forms.

There is, however, no need to postulate hybridization to explain the apparent failure of *T. rhodesiense* to spread more widely. A tsetse fly which has fed on an infected man and in which *T. rhodesiense* has developed in the salivary glands may feed on and infect several animals during its lifetime. Some of these animals may already be infected with *T. brucei* and some may become so later; the result may be a mixed infection, as there is no evidence of any differentiation between the two trypanosomes by animals other than man. Mixed infections may develop in tsetse flies which feed on these animals, as it is probable that the salivary gland trypanosomes are derived from more than one trypanosome and these mixed infections may be transmitted to other animals which may be, or may become later, infected with *T. brucei*

The result will be that the trypanosomes pathogenic to man will become "diluted" with non-pathogenic trypanosomes owing to the greater prevalence of the latter. When a tsetse fly with a mixed infection feeds on man, only a proportion of the inoculated trypanosomes will be pathogenic; when this proportion falls to a low level, then no infection would result because, as FAIRBAIRN and BURTT (1946) showed, man requires a minimum infective dose of *T. rhodesiense*. The result would be that *T. rhodesiense* in animals in natural conditions would tend to be "diluted" with *T. brucei* so that mixed infections of the polymorphic trypanosomes transmitted by a tsetse fly would be unable to infect man. In such circumstances animals might act as a reservoir of *T. rhodesiense* but in the absence of infections or re-infections by tsetse flies with "pure" *T. rhodesiense*, which for the most part would only be acquired from man, this action might only be temporary. The relative importance of man and animal infection might vary considerably in the conditions of different endemic areas.

Another factor which may be of importance in determining an area in which the disease may become endemic is the species of animals acting as hosts of the tsetse fly. ASHCROFT, BURTT and FAIRBAIRN (1959), as was mentioned previously, have shown that some species, *e.g.* warthog and bushpig, can be infected with *T. rhodesiense* and *T. brucei* but that the infections are slight and very much less persistent than infections in some other animals, *e.g.* bushbuck and reedbuck. In areas where warthogs are the main host of the tsetse fly, *T. rhodesiense* might never become endemic because of the resistance of the animals to the parasite.

It is interesting to note that WEITZ and GLASGOW (1956) and GLASGOW *et al.* (1958) found that in a *G. swynnertoni* and *G. pallidipes* belt in Shinyanga District, where sleeping sickness has never been diagnosed, the host of the tsetse fly is predominantly warthog. On the other hand, in Sakwa, in the Central Nyanza District of Kenya, where a few cases of *T. rhodesiense* sleeping sickness occur, the host of the tsetse fly, *G. pallidipes*, is mainly bushbuck (MCMAHON, personal communication) which has actually been shown by HEISCH, MCMAHON and MANSON-BAHR (1958) to carry *T. rhodesiense*. In another endemic area on the mainland of Busoga, Uganda, bushbuck and waterbuck are common and are probably the chief hosts of the vector of the disease, *G. pallidipes*. On Sigulu Island, another focus of the disease in Busoga, the only animal likely to act as a host of *G. pallidipes* is waterbuck. KINGHORN (1925), in the Luangwa Valley of Rhodesia, observed that waterbuck were very common close to the African villages and suggested that these animals might be the most dangerous reservoir of the disease.

An indirect means of studying the problem is to find the relative incidence of polymorphic trypanosome infections in the species of wild animals which may act as hosts to the tsetse fly. ASHCROFT (1959c) has summarized the main investigations of this type; of all species waterbuck have been found to have the greatest infection rate with polymorphic trypanosomes, which suggests that they must be particularly susceptible to them, and therefore, although other species should not be disregarded, are most likely to act as a reservoir.

Although these facts are incomplete, they do suggest that a systematic investigation might show that certain animal species are particularly common as hosts of the tsetse flies in areas in which *T. rhodesiense* sleeping sickness is endemic.

The epidemiology of sleeping sickness due to T. gambiense

Experimental evidence indicates that *T. gambiense* is poorly adapted in virulence to infect those wild animals which are hosts of tsetse flies. However, some work carried out in Uganda by Bruce and his collegues, and later by Duke, led to the belief that some antelope might be infected and act as a reservoir. This work is considered in some detail as the conclusions appear to be open to doubt, mainly owing to the fact that insufficient attention, understandable because at that time the similar morphology of *T. brucei* had only recently been emphasized, was paid to the differentiation of strains which might have been *T. gambiense* or *T. brucei*.

Bruce *et al.* (1911) inoculated 6 reedbuck, 3 bushbuck and one waterbuck with a strain of polymorphic trypanosomes derived from a person infected in the Uganda epidemic; the strain was presumed to be *T. gambiense* although no details are given of its virulence to laboratory animals. Trypanosomes were seen in the blood of all these antelope about 10 days after inoculation so there can be little doubt that they were infected. Duke (1912b) fed *G. palpalis* on the animals up to 22 months later and found that some of the flies became infected; he concluded, therefore, that *T. gambiense* had persisted for this time. Corson (1936c) pointed out that the animals might already have been infected with *T. brucei* when acquired for experiments as there was no record that they were captured in tsetse-free areas; the infection which persisted so long might have been a naturally acquired *T. brucei*, and the inoculated *T. gambiense* might, in fact, have died out. In a later communication, Duke (1912c) stated that the trypanosomes isolated 15 months after the initial infection of one of these reedbuck killed 3 monkeys (*Cercopithecus aethiops*) in 89, 111 and 176 days and 2 guineapigs in 50 and 68 days. The longevities of these animals are more like those of animals infected with a typical strain of *T. brucei* or *T. rhodesiense*, than with a typical strain of *T. gambiense*. Corson (1936b, 1937b, 1938c, 1939b) for example transmitted a strain of *T. gambiense* through monkeys (*Cercopithecus aethiops*) and of the 14 which died of trypanosomiasis only 1 lived less than 2 years and several survived for over 3 years. 160 monkeys of the same species have been infected with one strain of *T. rhodesiense* at Tinde Laboratory, Tanganyika (unpublished data); the average length of life of these monkeys was calculated for each year and found to vary from 60 to 185 days; 32 monkeys lived over 150 days. The average length of life of 14 guineapigs infected with the same strain of *T. rhodesiense* was 134 days; *T. gambiense* often fails to infect guineapigs. It must be emphasized, however, that the virulence of both *T. rhodesiense* and *T. gambiense* to animals is very variable and does not afford a rigid distinction between them, and that longevities of infected animals vary not only with the age, sex, species and method of maintenance but also with the mode of inoculation (fly feed or syringe) and with the infecting dose of trypanosomes.

Duke (1912a, 1912c) also described the isolation of strains of trypanosomes which he believed were *T. gambiense*, from sitatunga antelope from the Damba Islands of Lake Victoria. 5 years previously the population had been evacuated from these islands because of sleeping sickness and their return had been forbidden and Duke concluded that his strains were *T. gambiense* which had persisted in the sitatunga; he was not, however, able to test the infectivity of the strains to man and they may well have been *T. brucei*. A study (Duke, 1912c) of the longevities of laboratory animals infected with two strains from

sitatunga shows that the virulence of the strains was not typical of *T. gambiense*. DUKE (1921, 1932) again isolated some strains of polymorphic trypanosomes from Damba Island; on the last occasion they were shown to be non-pathogenic to man, and were therefore *T. brucei*. Eventually, after attempts to infect wild animals with *T. gambiense*, DUKE (1936), in a lucid exposition of the problems involved, changed his original views and concluded: "there can be no reasonable doubt that man is the principal reservoir of *T. gambiense* and that compared to him, domestic and game animals are negligible". This change in Duke's opinions does not seem to have been noted by all authorities and in some textbooks the work of Duke on Damba Island is still quoted and the impression is given that it has been shown that wild animals are important as a reservoir of *T. gambiense*.

Experimentally, it has been found without exception that *T. gambiense* is less virulent to all animals than is *T. brucei* or *T. rhodesiense*. KLEINE and ECKARD (1913) and DUKE (1928b) were able to infect sheep and goats with *T. gambiense* but sometimes with difficulty and the infection was self-limiting. VAN HOOF (1947) transmitted strains of *T. gambiense* cyclically by *G. palpalis* for several years through goats and pigs; the infections were benign, both animals recovering spontaneously. At Tinde laboratory (unpublished data) sheep and goats have been invariably killed by *T. rhodesiense* and *T. brucei*. It is well known that recently isolated strains of *T. gambiense* are less virulent to all laboratory animals than are strains of *T. brucei* or *T. rhodesiense*.

It has been mentioned previously that ASHCROFT, BURTT and FAIRBAIRN (1959) have shown that *T. rhodesiense* runs a transitory and benign course in those wild animals which are the hosts of tsetse flies. As *T. gambiense* is so much less virulent, it would be surprising if it could infect these animals or, if it did, the infection must be very scanty and in consequence it seems unlikely that these wild animals could act as a reservoir of *T. gambiense*. On the other hand, the animals which are highly susceptible to *T. rhodesiense* and *T. brucei*, *e.g.* Thomson's gazelles and monkeys, and which might be thought to be susceptible to *T. gambiense*, are not important sources of food for the tsetse flies (WEITZ and GLASGOW, 1956). It is possible, however, as VAN HOOF (1947) suggested, that the more susceptible domestic animals might, in certain circumstances, act as a reservoir.

It is not intended to give a comprehensive account of all the investigations into the epidemiology of sleeping sickness caused by *T. gambiense* which, owing to its wider distribution and greater incidence, has been more extensively studied than the *T. rhodesiense* disease. One of the most interesting and detailed studies was that of HUTCHINSON (1953a, b) in the Gambia. A typical example of his findings follows. In the Upper River Division of this territory, areas of high endemicity were found surrounding 3 side-creeks off the main river which were of great importance as foci of concentration of *G. palpalis* during the dry season. The people living close to these creeks came into exceptionally close contact with the tsetse fly in the dry season because they visited pools for bathing and washing. In contrast, the endemic incidence of the disease on the edge of the main river plains, where man-fly contact was interrupted and only took place in the wet season, was low. One aetiological factor of fundamental importance emerged from findings such as these, namely that the incidence and intensity of infection were determined by the type and the duration of contact which occurs between man and *G.*

palpalis. Where there was no contact between man and *G. palpalis* human trypanosomiasis did not occur; where contact was impersonal, occasional or interrupted the disease occurred only at a comparatively low level, even though the fly might be prevalent; but where the contact was personal, sustained and intimate a high incidence was encountered even when fly were not present in large numbers. The term "man-fly contact" needs elaboration. Tsetse flies may be prevalent and an individual man may be frequently bitten; the man-fly contact could therefore be said to be high, but to the individual fly man may be but an occasional source of food; this type of contact may be found in *G. morsitans*, *G. swynnertoni* and *G. pallidipes* fly belts and in some *G. palpalis* areas. Personal or intimate contact occurs when each individual fly feeds frequently on man and is found in *G. palpalis* (and probably *G. tachinoides*) areas only. Intimate man-fly contact is usually found in foci to which *G. palpalis* or *G. tachinoides* is confined by the vegetation and by the climate and which are frequently visited by the human population, often because they contain the only available source of water.

Morris (1951, 1952) reviewed the history of sleeping sickness in the Gold Coast. The epidemiology was explained on the basis of the movements of the human population and on their degree of contact with the riverine tsetse flies.

Morris (in press) has investigated the areas of endemic *T. gambiense* sleeping sickness in Uganda and Kenya and has found that the circumstances prevailing there were similar to those described by Hutchinson in the Gambia. Sleeping sickness persisted at a low endemicity in some localities where man had some contact with *G. palpalis* but when circumstances altered, leading to a more intimate man-fly contact, epidemics often broke out.

A very interesting experiment in man-fly contact has been carried out in Nigeria (WAITR, 1957). *G. palpalis* were marked, released and recaptured after 18 days at two water holes, one in Northern Nigeria, where sleeping sickness occurs and one in Southern Nigeria, where it is absent. It was found that the percentage of flies recaptured, which indicates the degree of man-fly contact, was much higher in the north than in the south in both the dry and wet seasons. The blood meals of *G. palpalis* captured in the northerly area were examined; 27% had fed on primates, most of whom were probably man, and 45% had fed on reptiles; only 26% had fed on mammals other than man.

The evidence, both experimental and epidemiological, indicates that *T. gambiense* is principally a parasite of man and the epidemiology of this form of sleeping sickness can be explained by the habits of the vector tsetse fly and the human population without considering those of wild animals.

The distribution of T. gambiense and T. rhodesiense

The conclusion has been reached that *T. rhodesiense*, although distinct from *T. brucei*, can infect some wild animals which may act as a reservoir; in contrast, *T. gambiense* is principally a human parasite and is transmitted from man to man. These conclusions will now be shown to be consonant with the distribution of the two types of human trypanosomiasis and with the bionomics of their vectors.

One of the most striking features of the epidemiology of human trypanosomiasis is the apparent inability of the game tsetse flies, *G. morsitans*, *G.*

swynnertoni and *G. pallidipes*, to act as vectors of *T. gambiense*, although they act as vectors of *T. rhodesiense*. The riverine tsetse flies, *G. palpalis* and *G. tachinoides*, on the other hand, transmit *T. gambiense*.

T. gambiense sleeping sickness advanced up to tributaries of the Congo infested by *G. palpalis* at the end of the 19th century but halted on reaching the limit of *G. palpalis* beyond which lay the game tsetse-fly belts. KLEINE and TAUTE (1911) studied an epidemic of *T. gambiense* sleeping sickness on the east shores of Lake Tanganyika; they observed that the disease occurred in *G. palpalis* but not in the closely adjoining *G. morsitans* areas. At the present time (APTED, 1956) a small focus of *T. gambiense* disease is found on the coast of Lake Tanganyika just north of Kigoma—the vector is *G. palpalis*; *T. gambiense* sleeping sickness is not found in the huge adjacent areas of *G. morsitans*, where *G. palpalis* is absent and where the disease due to *T. rhodesiense* is not uncommon. RODHAIN *et al.* (1913) observed that *G. palpalis* but not *G. morsitans* was the vector of *T. gambiense* in the Katanga Province of the Belgian Congo, where both species of tsetse fly were present. HUTCHINSON (1953a, b) found that, in the Gambia, patients with *T. gambiense* acquired their infections in areas where *G. palpalis* existed but never where *G. morsitans* was the only species of tsetse fly.

The absence of *T. gambiense* from the game tsetse-fly belts is, at first sight, rather surprising. Sleeping sickness due to *T. gambiense* is usually less severe and the disease takes a much longer and more chronic course than that due to *T. rhodesiense*. If man was the sole host of both trypanosomes, the chances of contact between tsetse flies and a person infected with *T. gambiense* would be greater than the chances of contact between tsetse flies and a person infected with *T. rhodesiense*. Why then do the game tsetse flies, which are less likely to feed on man than the riverine tsetse flies, act as vectors of *T. rhodesiense* but not *T. gambiense*?

At the beginning of this century when the prospect of *T. gambiense* advancing into the great belts of these tsetse flies in eastern and central Africa was viewed with considerable alarm, it was hoped that the answer would prove to be that the human trypanosome was incapable of development in the game tsetse flies. TAUTE (1911), however, showed that *T. gambiense* could develop in *G. morsitans* in the laboratory, and KLEINE and FISCHER (1913) found that trypanosomes developed in a greater proportion of *G. morsitans* than *G. palpalis* when these flies were fed on monkeys infected with *T. gambiense*.

Attention has been paid to the possibility that the properties of *T. gambiense* may be altered by the game tsetse flies to those of *T. rhodesiense*. CORSON (1936b, 1937b, 1938c, 1939b) investigated this possibility by transmitting a strain of *T. gambiense* through monkeys by *G. morsitans*; in $4\frac{1}{2}$ years no change was detected in the virulence of the strain. WILLETT (1956a, b, c) has suggested, but without providing any direct evidence, that transmission through *G. pallidipes* may convert *T. gambiense* into *T. rhodesiense*.

ASHCROFT (1959a) has put forward the view that the distribution of *T. gambiense* and *T. rhodesiense* is not brought about by any alterations in the trypanosomes caused by different species of tsetse flies acting as vectors, but by differences in mammalian hosts. The riverine tsetse flies, *G. palpalis* and *G. tachinoides*, which are the vectors of *T. gambiense*, can exist in the presence of man who can be an important source of food for them; they are able

therefore to transmit trypanosome infection from man to man without the intervention of any other mammalian host. In these circumstances *T. gambiense* has an advantage over *T. rhodesiense* because a man infected with the former would continue, in view of the relatively symptomless nature of the infection, to visit the haunts of the tsetse fly, while a man infected with the latter would be more sick and confined to his dwelling out of contact with the fly. It would therefore be expected that natural selection would result in *T. gambiense* and not *T. rhodesiense* being the trypanosome transmitted by the anthropophilic tsetse fly. The game tsetse fly on the other hand are zoophilic and they rarely feed on man, who is an incidental host only and whose presence and settlement result in their absence; in these circumstances *T. gambiense* would not be transmitted because of its inability to infect the animal hosts of the tsetse fly whereas *T. rhodesiense* could be transmitted from animal to animal with an occasional infection of man.

If this explanation is the true one, then it would be expected that the riverine tsetse flies would act as vectors of *T. rhodesiense* in circumstances in which they were feeding chiefly on animals to which *T. rhodesiense* is suitably adapted, and rarely on man. There is, however, no direct evidence that they do act as vectors of *T. rhodesiense*, although the isolation by LESTER (1933) of strains with intermediate characteristics is suggestive, but it is possible that cases of this type of sleeping sickness have been overlooked because of the far greater prevalence of the *T. gambiense* type. Thorough investigation of strains from some riverine tsetse-fly areas might demonstrate the presence of *T. rhodesiense*.

The suggestion can be expressed in another way: tsetse flies can only act as vectors of those trypanosomes which are suitably adapted to the principal hosts of the tsetse flies; if the trypanosomes are too virulent, then the hosts will quickly sicken or die and fly-trypanosome contact will be lost; if the trypanosomes are not sufficiently virulent, then so few parasites will be present in the blood that the fly will not pick up trypanosomes. In the case of the riverine tsetse flies whose host is man, *T. gambiense* is quite well adapted to man but *T. rhodesiense* is too virulent; in the case of the game tsetse flies *T. rhodesiense* is adapted to the game but *T. gambiense* is not sufficiently virulent. This explanation for the distribution of the two types of human trypanosomes seems to be in accord with general principles of host-parasite relations. It does not exclude the possibility that some species of animals—wild or domestic—might be a reservoir of *T. gambiense* if they were susceptible to the parasite. It could account for the existence of strains with properties intermediate between those of *T. gambiense* and *T. rhodesiense* by the possibility that the tsetse flies were feeding on certain animals and man in approximately equal proportions. Its basic proposition is that a trypanosome, for successful survival, must be so adapted in its virulence to the chief hosts of the tsetse fly that sufficient contact between the trypanosome and the fly can be maintained.

The relationship between T. brucei, T. rhodesiense and T. gambiense

The relationship between the three trypanosomes, *T. brucei*, *T. rhodesiense* and *T. gambiense* has been so much discussed that the subject is approached with diffidence. It is not intended to give a full account of suggestions put forward by many authorities. Some of these can be found in YORKE (1920),

DUKE (1921, 1928a, 1933, 1935a, b, 1937b), KLEINE (1923, 1928), WENYON (1926), YORKE, ADAMS and MURGATROYD (1930), LESTER (1933), BRUMPT (1936), HOARE (1943), FAIRBAIRN and BURTT (1946), SANDGROUND (1947) and WILLETT (1956b, c). Generally speaking the various viewpoints differ mainly on the relationship between *T. brucei* and *T. rhodesiense* and whether there is any distinct difference between these two trypanosomes. It has already been shown that the bulk of the evidence indicates that *T. brucei* and *T. rhodesiense* are distinct but the relationship between *T. rhodesiense* and *T. gambiense* remains to be discussed.

As has been noted, *T. rhodesiense* was distinguished from *T. gambiense* by STEPHENS and FANTHAM (1910, 1912) by its greater virulence to man and animals and by the presence of trypanosomes with posterior nuclei in the infections of small laboratory animals. Later it was found to be less sensitive than *T. gambiense* to arsenical drugs and less resistant to the trypanocidal action of human serum, both *in vitro* and *in vivo*, in the infections of rats and mice. However, it is now known that the distinction between the two trypanosomes is less well marked than was once believed.

KLEINE (1928) and LAVIER (1928) found that posteronuclear trypanosomes do occur, although rarely, in *T. gambiense* infections. The rarity of posteronuclear forms may be connected with low level of parasitaemia in *T. gambiense* infections. ASHCROFT (1957) found, as have some previous workers, that changes in the morphology of *T. brucei* and *T. rhodesiense* were related to the remissions and relapses in the infections of rats; stumpy and posteronuclear forms were most abundant when the concentration of trypanosomes in the blood was decreasing. WILLETT (personal communication) examined Ashcroft's data and pointed out that the greater the proportion of stumpy forms, the greater the proportional decrease in the parasitaemia in the next 24 hours and the greater the proportion of posteronuclear forms among the stumpy forms. It seems probable, therefore, that the influence which gives rise to stumpy forms gives rise, when it acts more powerfully, to posteronuclear forms. Ashcroft suggested that antibodies elaborated by the host resulted in the formation of stumpy forms; posteronuclear forms may therefore occur when antibodies rise to high concentrations quickly. It is reasonable to suppose that antibodies are produced in greater quantity and more quickly when the parasitaemia rises to high levels, as it does in *T. brucei* and *T. rhodesiense* infections, than when the parasitaemia is of low intensity as in infections due to *T. gambiense*. The differences in the number of posteronuclear forms may be connected merely with physiological differences in virulence.

LESTER (1933) isolated several strains from patients in Nigeria and tested their virulence, resistance to human serum and sensitivity to drugs; he concluded that some of the strains were not entirely characteristic of *T. gambiense* or *T. rhodesiense*, but were transitional. There does not appear, then, to be any absolute clear-cut distinction between *T. rhodesiense* and *T. gambiense*, which suggests that both may be basically the same parasite and that their physiological differences may have arisen because they may exist under different conditions.

It is well known that strains of trypanosomes undergo marked changes when syringe-passaged for a long time through laboratory animals (see DUKE (1934), MURGATROYD and YORKE (1937), FAIRBAIRN and CULWICK (1947),

FAIRBAIRN (1956), JENKINS and GRAINGE (1956) and ASHCROFT (in preparation)); BRUCE (1914) vividly expressed these changes when he wrote " it seems to me to be as dangerous to classify trypanosomes from old laboratory strains as it would be to give the natural history of the blue rock pigeon from a study of our tame variety ".

SANDGROUND (1947) converted a strain of *T. gambiense* into a strain which, in virulence to laboratory animals and in its reactions to drugs was similar to a laboratory strain of *T. brucei*, by 7 syringe-passages through 7-day-old rats. ASHCROFT (1959b) found that a strain of *T. brucei* maintained in sheep was more virulent to adult than to young rats; the strain was then syringe-passaged through young rats for 4 months and its relative virulence to young and adult animals became reversed, so that it was then more virulent to younger than to older rats.

Changes have been reported not only in syringe-passaged but also in fly-transmitted strains. FAIRBAIRN and BURTT (1946), WILLETT and FAIRBAIRN (1955) and ASHCROFT (1959a) showed that the virulence of a cyclically transmitted strain of *T. rhodesiense* was influenced by the species of host animal through which it was passed.

These experiments demonstrate the plasticity of strains of polymorphic trypanosomes and suggest that the difference in host animals may cause the differences between *T. gambiense* and *T. rhodesiense*. The evidence already considered indicates that *T. rhodesiense* is a parasite of animals as well as man but that *T. gambiense* is principally a parasite of man. It seems reasonable to suppose that *T. gambiense* has acquired its properties because it has become adapted to man, whereas *T. rhodesiense* is adapted to animals. The relationship between the three trypanosomes may therefore be summed up thus; *T. gambiense*, *T. brucei* and *T. rhodesiense* are morphologically identical but with different physiological properties and, strictly speaking, as HOARE (1943) concluded, they may be regarded as biological races of the same species. *T. gambiense* and *T. rhodesiense* may be said to be more closely related because it appears that there is no constant distinction between them such as there is between *T. brucei* and the other two. On the other hand, *T. brucei* and *T. rhodesiense* resemble each other closely in almost all physiological characteristics because both are primarily parasites of animals whereas *T. gambiense* is primarily a parasite of man.

SUMMARY

1. The discovery of the morphologically identical polymorphic trypanosomes, *T. brucei*, *T. gambiense* and *T. rhodesiense*, is briefly described.
2. The controversy over the relationship between *T. brucei* and *T. rhodesiense* is discussed. The absence of *T. rhodesiense* sleeping sickness from some areas where *T. brucei* is present in animals and the stability of the pathogenicity to man when strains are transmitted experimentally through animals indicate that the two trypanosomes are distinct.
3. Wild animals act as a reservoir, the importance of which is difficult to estimate, of *T. rhodesiense*, as shown by their experimental infection, by the isolation of the trypanosome from *G. pallidipes* and from a bushbuck, and by epidemiological studies.

4. Certain species of wild animals are particularly susceptible to *T. rhodesiense* and its distribution may be limited to areas where these species are important hosts of the tsetse fly.
5. Wild animals may be unable to act indefinitely as a reservoir of *T. rhodesiense* without re-infection from man because the greater prevalence of *T. brucei* may lead to so much dilution of *T. rhodesiense* that naturally occurring mixed strains may become non-pathogenic to man.
6. The epidemiological pattern of *T. gambiense* sleeping sickness is that of a disease transmitted from man to man, in which the degree of intimate contact with the tsetse-fly vector is all important. Experimental and epidemiological evidence does not indicate that wild animals play any important part in the transmission.
7. *T. gambiense* is transmitted by the riverine tsetse flies and *T. rhodesiense* by the game tsetse flies. This distribution can be understood if only those strains can be transmitted which are so adapted in virulence to the important hosts of the tsetse flies concerned that contact between fly and trypanosome can be maintained. *T. rhodesiense* is adapted to some wild animals which are important hosts of the game tsetse flies and *T. gambiense* is fairly well adapted to man, who is, in sleeping sickness areas, an important host of the riverine tsetse flies. *T. rhodesiense* is poorly adapted to man as is *T. gambiense* to wild animals.
8. The relationship between *T. rhodesiense* and *T. gambiense* is discussed. The absence of any absolute differences together with the experimental evidence showing that the properties of trypanosomes are influenced by their mammalian hosts, suggest that there is one polymorphic trypanosome which is able to infect a wide range of animals including man and that it has the characteristics of either *T. gambiense* or *T. rhodesiense* according to whether its principal hosts are man or wild animals, which will depend on the species of tsetse fly acting as vector.

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SUMMARY OF RECENT ABSTRACTS*

IX. LEPROSY†

General

In a collection of papers published in *Maroc Méd.* (p. 514) various subjects are discussed, including resistance and susceptibility to the disease, treatment, clinical matters including changes in the lungs, bones and eyes, and the bacteriology and pathology of the disease. Most of the work has been described before, but the symposium is a useful summary.

In a special issue of *Leprologia* (p. 771) there is a symposium on the subject of the immunological relationships between leprosy and tuberculosis. Several speakers advocated BCG. Basombrío *et al.* referred to the low rate of conjugal leprosy. Castro and Arcuri found that an antigen from the whole proteins of a leproma is sufficiently sensitive for the Fernandez reaction and has the advantage that it does not itself sensitize, as the whole bacillary antigen does. Basombrío *et al.* did not find highly diluted Mitsuda antigen satisfactory for testing the resistance of contacts—the undiluted antigen revealed far more positive results. Bergel discusses the antioxidant action of DDS. Various other authors discussed a wide range of subjects.

In the *Rev. Brasileira Leprologia* (p. 1124) there is an account of a symposium on BCG and leprosy. This was not the occasion for the presentation of new work, and the views expressed by the different speakers have been expressed before. But it is a valuable summary of current opinion, and on the whole is in favour of BCG. The biological association between tuberculosis and leprosy is complicated, but is recognized.

Epidemiology

Davey (p. 517) notes that there are clinical resemblances between some of the lesions of leprosy and yaws, and discusses differential diagnosis. Epidemiologically there is much resemblance between these diseases: both are chronic and are spread by contagion, both are rural and are connected with a low standard of living and hygiene, both declined with the introduction of clothing, in both children are more susceptible than adults, conjugal infection is rare and congenital spread is unknown. Both are associated with the tropics and show seasonal variations.

In a study of young children of leprous parents Souza Campos *et al.* (p. 410) conclude that when tuberculous infection precedes leprosy contagion it usually induces resistance to leprosy, but when leprosy infection comes first there is increased susceptibility to tuberculous infection, as shown by the high index of tuberculin hypersensitivity in lepromatous leprosy. A study of the lepromin reaction indicates that the incidence of leprosy in close contacts is much higher than is indicated by the epidemiological data.

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* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1958, v. 55. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

† For previous articles on leprosy in this series see the November issues of the *Tropical Diseases Bulletin* each year since 1939.

CHAUSSINAND (p. 1234) elaborates his view that there is antagonism between tuberculosis and leprosy which is reflected in the fact that in Portugal (for instance) the places with high tuberculosis rates have low leprosy rates, and *vice versa.* He points out that tuberculin allergy only indicates infection, whereas lepromin allergy is an indication of immunity, being a kind of Koch phenomenon as a reaction to injected bacilli. An analogous test in tuberculosis would require an antigen of killed bacilli, not of tuberculin.

ANDRÉ and ANDRÉ-GADRAS (p. 51) quote evidence from Gabon which suggests that heterozygous sicklers are less liable to suffer from malignant leprosy than normal homozygotes.

In a survey in part of Uganda NELSON (p. 769) found the incidence of leprosy to vary from 0·6 to 53·3 per 1000, 18·4% being lepromatous and 72·6% tuberculoid. Incidence was much higher below 4000 feet than at greater altitudes where rainfall was heavier and population more dense, and these features therefore do not seem to be important. At the lower altitudes the scattered population is relatively primitive and has had the least contact with civilization, and tuberculosis is uncommon; these factors may explain the higher incidence of leprosy. The incidence of leprosy found by WORSFOLD (p. 167) in part of Northern Rhodesia was 11·85 per 1000, rather more in adult women than in men (who tend to leave the area for work). One quarter were lepromatous. Treatment with DDS was excellent.

GALEA and BONNICI (p. 48) give an account of the history of leprosy in Malta. The incidence was 0·54 per 1000 in 1913, and 0·45 in 1956, with a lepromatous rate of 66%. The system of compulsory segregation has been abandoned.

UTKU (p. 49), discussing leprosy in Turkey, shows that endemic regions exist in eastern, central and northern areas. Compulsory isolation is the rule, but increases the difficulty in finding cases.

MULLICK *et al.* (p. 1333) give an account of an area of West Bengal served by an investigation centre, in which there was some increase in leprosy in the period 1937–56.

In the Gifu Prefecture of Japan leprosy is predominantly a rural disease, and KITANO (p. 1333) states that in about one-quarter of the cases reported in 1936–55 the infection was familial.

MORÁN ORDOÑEZ (p. 49) reports on central Mexico where the incidence of leprosy does not seem to be falling. It is commonest in rural areas and in agricultural labourers.

In Martinique MONTESTRUC *et al.* (p. 1338) comment on the frequency of collateral as opposed to conjugal infection and emphasize the susceptibility of children. The tuberculoid form, which occurs in most resistant patients, is the least common in young subjects; the incubation period is particularly short in very young infants. The authors suggest means of control, which include BCG and careful supervision of contacts.

The Relationship between Leprosy and Tuberculosis

DAVEY *et al.* (p. 770) report a tuberculin and lepromin survey in Nigeria, and recognize a relationship between the sensitivities to these in schoolchildren. In towns it is possible that tuberculous infection is responsible to a small extent for sensitivity to lepromin, but in rural areas where tuberculosis is less

frequent there is no evidence that it has any appreciable influence on lepromin sensitivity. In some areas it is doubtful if *Myco. leprae* itself could be responsible for the level of lepromin sensitivity found in young children, and geographical and constitutional factors are probably involved.

In a group of children who had been in contact with leprosy patients, and who were tested with tuberculin and lepromin, MONTESTRUC *et al.* (p. 1123) found 65% negative to both tests; these should be vaccinated with BCG. 23·4% were positive to tuberculin and negative to lepromin, and they should be vaccinated only if careful examination fails to show tuberculous lesions. The remainder were positive to lepromin and either positive or negative to tuberculin; those negative to tuberculin need careful watching, most of them were in contact with lepromatous patients.

In an investigation of lepromin by the agar-diffusion method with sera of leprosy patients, BURRELL and RHEINS (p. 1336) observed that sera from lepromatous patients gave 2 lines of precipitation, and from tuberculoid only 1. Lepromatous, tuberculoid and anti-BCG sera contain a common antibody, and sera which react to lepromin can be neutralized with tuberculin. There is a common antibody to tuberculin in lepromatous and anti-BCG sera, but not in tuberculoid sera. In experiments on dogs OLMOS CASTRO and ARCURI (p. 1131) observed that there is a cross sensitization between BCG and lepromin. The cross sensitization to lepromin induced by inoculation of BCG is non-specific and transitory (it may disappear in 9 months); the cross sensitization to BCG induced by lepromin is more stable. The specific sensitization induced by either lepromin or BCG is equally stable.

It is known that the lepromin reaction becomes positive in a proportion of persons never in contact with the disease, and DOULL *et al.* (p. 410) have shown that this may be brought about by injection of BCG, though the lepromin used in the preliminary test [see SOUZA CAMPOS below], and certain other factors which are not understood, are partly responsible. CAPURRO *et al.* (p. 522) found that in a majority of subjects inoculated with a vaccine of *Myco. tuberculosis* irradiated with ultra-violet rays, the formerly negative lepromin reaction was converted to positive.

COLLIER *et al.* (pp. 171, 521, 1336) found the Fernandez and Mitsuda tests negative in the majority of a group of leprosy patients (L I, II and III) but positive in the majority of a group of tuberculous patients. The Essen antigen is prepared from human *Myco. tuberculosis* and does not react with Wassermann-positive sera. These authors used it quantitatively in a complement-fixation test and found the test positive more often and in higher titre in lepromatous than in tuberculoid leprosy. The titre declined as the disease improved.

RHEINS *et al.* (p. 521) describe the results of haemagglutination and haemolysis tests in Filipino schoolchildren in a leprosy area. For these tests sheep erythrocytes were sensitized with Old Tuberculin, and sera were inactivated and adsorbed twice with sheep cells to remove naturally-occurring antibodies. 40% of the sera contained haemagglutinating antibodies and 85% of the subjects gave positive lepromin reactions. In a considerable series of investigations on lepromatous leprosy ROY and BANERJEE (p. 172) found that there was no correlation between the haemagglutinin reaction and skin sensitivity to tuberculin in patients with clinical leprosy.

Lepromin Test

ROTBERG (p. 50) postulates the N factor— potential natural immunity— which most children possess at birth, and by virtue of which they gradually develop resistance; as is shown when the original negative lepromin becomes strongly positive. This change of potential to actual resistance may be increased by infection with tuberculosis or BCG. Some children, however, do not possess this factor and they cannot develop resistance; it is in these that lepromatous disease develops, though not in all. These anergic subjects do not develop positive lepromin tests after BCG, and they are the only potential spreaders of infection. BECHELLI *et al.* (p. 50) in part of Brazil observed a moderate proportion of positive lepromin tests in recent Dutch immigrant children, possibly because they possessed the N factor of Rotberg, and were sensitized. COLLIER (p. 1126) in discussing the lepromin test argues that the negative result in lepromatous disease is due to allergic paralysis, the small amounts of antibodies that might have been formed having been swamped by excess of antigen. This paralysis is caused by components of *Myco. leprae.* He does not accept the idea of Rotberg's N factor.

SOUZA CAMPOS (p. 522) sums up the opinions of many workers (but not all) to the effect that repeated injection of lepromin tends to convert a negative to a positive reaction. In experiments with healthy persons OLMOS CASTRO and ARCURI (p. 1233) found that a single injection of integral lepromin can sensitize over 50% previously negative to the Fernandez reaction.

Aetiology

CHATTERJEE (p. 1239) inoculated *Myco. leprae* from lepromatous leprosy, separated carefully from the human tissue, into hybrid black mice and hamsters, and observed appearances strongly suggesting that the organisms had multiplied in the mice. Lepromin prepared from the affected mice gave positive results in tuberculoid patients. In comment Muir remarks on the importance of this work. BERGEL (pp. 172, 414, 527) quotes experiments which indicate that when *Myco. leprae* were inoculated into rats fed on pro-oxidant diet (low in vitamin E and containing 15% linseed oil), the bacilli showed signs suggestive of multiplication, which were not observed in control rats. Later intratesticular subinoculation into other rats on the same diet showed abundant evidence of multiplication, and a third inoculation was planned. It seems that for the first time the most important of Koch's postulates has been fulfilled with the leprosy bacillus. The author continued these experiments and found that the third subinoculation also produced signs of multiplication which were entirely absent in rats on normal diet. There was no evidence that the bacilli observed were anything but *Myco. leprae*, and this seems to be the first time that this organism has been cultivated *in vivo* outside the human body.

NOEL and MARIE-SUZANNE (p. 1123) describe appearances in the chorioallantoic membrane of chick embryos inoculated with *Myco. leprae* or *Myco. marianum,* which suggest multiplication of these organisms.

WADE (p. 519) describes a modification of the formaldehyde method for staining acid-fast bacilli in paraffin sections; details are given in the abstract. KOOIJ (p. 518) reports an electron microscope study of the morphology of *Myco. leprae.*

By irradiation of excised portions of lepromatous tissue with X-rays

MUKHERJI (p. 523) has been able to show that it is possible to affect the bacilli without damaging the tissue cells.

Pathology

CHATTERJEE *et al.* (p. 168) discuss the histology of skin lesions in lepromatous leprosy as revealed by cytochemical techniques.

ISHIHARA (p. 1335) has recognized giant cells in the skin in lepromatous and tuberculoid leprosy and in reactional erythema nodosum leprosum, and inclusion bodies in them in all except the tuberculoid form.

MUKERJEE and GHOSAL (p. 168) used an acid phosphatase technique, with Ziehl-Neelsen staining, for studying nerve tissue in leprosy. Details of the findings should be sought in the original.

Electron microscope studies made by NISHIURA *et al.* (p. 1231) show that in lepromatous peripheral nerves leprosy bacilli may be found within the axons, apparently phagocyted by the axons and not by the Schwann cells.

MICHMAN and SAGHER (p. 1127) discuss the changes in the anterior nasal spine and the maxillary bone in leprosy.

CHATTERJEE *et al.* (p. 411) investigated a loosely-bound calcium-phosphate-lipoid complex found in the skin in lepromatous leprosy.

GOKHALE (p. 1232) found an increased content of histamine in the blood, especially marked in the tuberculoid form, which may indicate a connexion with the lepromin test, characteristically positive in this form.

A study of cholesterol, the lipoproteins, glycoproteins and uroproteins in the sera of patients with leprosy is reported by TARABINI (p. 1018). Serum albumin is usually decreased and globulin increased, and this disproportion leads to deposit of paraproteins (especially amyloid substance) in the organs. Renal disease in leprosy is thought to be largely the result of amyloid disease of the kidney. DE VITA and BINI (p. 1231) found diminution in serum albumin in severe leprosy, and some increase in the globulins.

Various Tests

KOOIJ and GERRITSEN (p. 1019) compare lepromin with the Kveim antigen, which is prepared in a similar manner from sarcoid tissue, and gives a positive result in sarcoidosis when injected into the skin. It is known that suspensions of normal organs can give similar results in sarcoidosis, and the authors therefore attempted a similar experiment in leprosy by injecting preparations from normal skin and liver. They found that these substances gave positive reactions in tuberculoid leprosy and negative in lepromatous. The Mitsuda reaction therefore seems to be a kind of foreign body reaction. The skin of patients with psoriasis and other skin diseases reacts to various stimuli in a manner characteristic of the particular disease, and WAALER (p. 1126) claims that the same is true of leprosy, basing his findings on histological examination after injection of tuberculin; for instance, in active lepromatous disease the reaction was lepromatous.

ROSSETTI *et al.* (p. 1019) confirm previous work to the effect that the TPI test is negative in leprosy, and discuss the causation of false positive results in the various classical complement-fixation and flocculation tests. OLITZKI and SAGHER (p. 170) used the Kahn universal reaction in patients with lepromatous or non-characteristic leprosy under treatment. Some gave strong reactions in

Zone I, weaker in Zone III, and feeble or negative in Zone II. The asymmetrical curve tends to appear early when improvement occurs under treatment. In the Philippines ZARCO and CHAN (p. 1232) tested leprosy patients (mostly mixed cutaneous) with various tests for syphilis finding 52·7% positive to the Kahn, and fewer to the other tests. COLLIER and BUENO DE MESQUITA (p. 1233) did the same, finding that lepromatous patients gave more positive results than tuberculoid. The results of leprosy complement-fixation tests (Essen antigen) are closely similar to those of the syphilis tests, but the authors claim that the positive syphilis and leprosy tests are independent of each other.

Clinical Findings

DE GRAUWE and VERDIN (p. 169) comment on the value of cutaneous biopsy in the diagnosis of leprosy and the control of treatment. Clinically cured patients are sometimes shown by biopsy still to be positive. CAMAIN *et al.* (p. 170) found puncture biopsy of the liver to be positive in the majority of lepromatous patients examined in this way, but less often in tuberculoid and indeterminate cases. They describe the appearances found.

After observing a considerable number of patients with erythema nodosum leprosum, which developed during treatment of lepromatous leprosy, and comparing their progress with that of control patients, DAVISON and KOOIJ (p. 526) conclude that this is not a favourable sign.

In describing tuberculoid leprosy in a pair of identical twins, the only infected members of a family of 9, who were probably infected by an outside relative, BROWN and STONE (p. 518) suggest that the fact that they were the only members of the family to become infected, though all were equally exposed, confirms the existence of a constitutional factor in resistance, which determines whether successful invasion will take place.

OGATA (p. 1334) discusses temperature regulation in leprosy which is seriously affected by the loss of the skin functions—sensation, sweating and vasomotor activity—in leprosy. The products of destroyed body tissues may accumulate much more in leprosy than in normal persons, and histamine-like substances will increase in body fluids, and changes in body fluids influence the regulation of body temperature. Various metabolic studies are recorded.

FRUGONI (p. 1020) discusses the lesions of the ear, nose and throat in leprosy as seen in the Yemen, noting that in many cases the cause of death is inhalation pneumonia due to anaesthesia of the pharynx and larynx following lepromatous infiltration.

KINNEAR and DAVISON (p. 520) could not find any correlation between gynaecomastia and liver dysfunction or oestrogen excretion in leprosy.

HOLMES (p. 523) found lesions of the eyes in 10% of leprous patients in South Korea, and gives advice on the organization of treatment.

Treatment

RIDLEY (p. 525) describes his method of estimating progress in the treatment of leprosy by examining serial biopsy specimens and calculating the bacillary index by a standard technique.

In a discussion of chemotherapy BERGEL (p. 1337) mentions that the various drugs found effective have had an anti-oxidant effect and the power to

inactivate heavy metals; chaulmoogra is also liposoluble. In seeking new drugs these factors should be borne in mind.

DOULL *et al.* (p. 1128) conducted an extensive trial of diasone alone, diasone with isoniazid, isoniazid with streptomycin, and streptohydrazid, in lepromatous leprosy. All were well tolerated and clinical improvement was approximately the same for all, though bacteriological improvement was more marked in the Philippine series than in the African series. Much of the bacteriological improvement was probably not attributable to treatment, but to unknown causes not equally operative in all groups.

PODDAR and CHATTERJEE (p. 412) note that DDS is preferentially concentrated in the affected tissues of leprosy patients, and quote findings with DDS labelled with radio-active sulphur, which show the microscopic distribution in blood vessels and nerves. FLOCH *et al.* (p. 659) show that monoethyl sulphone is transformed to a large extent into DDS in the body, and probably acts by virtue of the DDS formed, though perhaps also to a certain extent by virtue of its own molecule. DAVISON (p. 52) has found that a soluble sulphone (Avlosulfon Soluble) given by injection twice each week is as good as, or better than, DDS by mouth, but has the disadvantage that it must be injected intramuscularly.

MCKENNA and CHALMERS (p. 526) report a case of dermatitis herpetiformis in which treatment with DDS, rising from 50 mgm. daily to 100 mgm. within one week, was followed by agranulocytosis. In comment Muir warns of the danger of increasing the dose too rapidly or too high.

From Madras EKAMBARAM (p. 774) writes of the advantage of sulphetrone (low toxicity, fairly rapid action) and its disadvantages (the need for injections twice each week, and the expense).

DREISBACH and COCHRANE (p. 1236) used streptohydrazid in lepromatous leprosy with good effect, but the results were better when sulphetrone was used as well.

SCHUJMAN (p. 1235) has observed that nerve damage often occurs during sulphone treatment of lepromatous leprosy, but that this can be arrested if chaulmoogra is injected over long periods in adequate dosage (20–30 cc. each week).

TOUZIN and BOCAT (p. 1021) have used Hyrgathione, a 25% suspension of DDS in ethyl esters of chaulmoogra with guiacol and aluminium monostearate, and by injecting 8 cc. (= 2 gm. DDS) each month have been able to maintain a sufficient blood concentration. To avoid the titre rising too high it may be necessary occasionally to suspend treatment. Good results were found by LAVIRON *et al.* (p. 412) with intramuscular injection of DDS suspensions every month, in chaulmoogra or in agar, but the minimum monthly dose should be 2 gm. They (p. 412) used thiacetazone in chaulmoogra in a weekly dose of 750 mgm. by injection, and found that side effects reported by other workers did not develop. The results were comparable with those obtained with sulphones and the drug could be used where there is intolerance or resistance to sulphones, but it is 3 times as expensive.

Cycloserine has been tried in lepromatous leprosy by DE ALMEIDA NETO and DE PAULA E SILVA (p. 53), but further experience is needed before definite conclusions can be drawn. BEISSÈGE *et al.* (p. 276) tried cycloserine in lepromatous leprosy, with encouraging clinical and bacteriological results; it is capable of producing improvement in patients who have ceased to improve

under sulphone treatment. A small-scale trial of cycloserine by PARDO CASTELLÓ (p. 1338) indicated that it is an excellent addition to the treatment of leprosy.

Favourable results in lepromatous and tuberculoid leprosy are reported by LAVIRON *et al.* (p. 1021) with the thioamide of isonicotinic acid.

DAVEY (p. 524) reports very favourably on diphenyl thiourea (DPT or SU 1906) in Nigeria, where he has used it for several years. Few side effects have been observed, and improvement in the condition of the patients has been continuous. The drug is administered by mouth daily—administration twice each week involving some loss of efficiency—and this is a disadvantage compared with DDS. Combined treatment with DDS and DPT was better than treatment with DDS alone; a combination of DPT and isoniazid was tried but though some results were very good, others were less so.

JOPLING and RIDLEY (p. 1237) used Vadrine (S. 131) by mouth in lepromatous leprosy, finding the results to be about the same as with DDS, but a longer period of trial is needed. BRODHAGE (p. 1237) used Vadrine in rat leprosy and observed a therapeutic action more effective than that of DDS.

ORBANEJA *et al.* (p. 52) tried a new preparation (Leprosan) in leprosy of various kinds, and though unable to assess its value, consider it worthy of further trial.

It has been claimed that injections of *Mycobacterium marianum* antigen in lepromatous patients may convert a negative lepromin reaction to positive. RELVICH (p. 54) used this antigen for periodical injection in patients receiving sulphones, but there was no obvious advantage over controls receiving sulphones only, though the author advocates further work. TOLENTINO (p. 1238) used injections of *Myco. marianum* vaccine in addition to DDS in lepromatous leprosy, but there seemed to be no advantage over DDS alone.

RODRIGUEZ (p. 1235) points out that the use of sulphones has increased the incidence of lepra reaction, and describes one form in which there are deep-seated subcutaneous nodules and chronic fibrous masses. It occurs most frequently in advanced stages of leprosy.

JONQUIERES (p. 53) used prednisone in reacting tuberculoid leprosy, continuing sulphone treatment at the same time. The reactions subsided rapidly. DE LAS AGUAS (p. 1022) reports good results from the use of prednisone in patients with various forms of the lepra reaction. For reactional conditions in tuberculoid leprosy LEWIS *et al.* (p. 1128) found cortisone together with DDS valuable, but the length of the treatment was greater than with potassium antimony tartrate, and they are chary about advocating it, chiefly because of expense.

MERKLEN and RIOU (p. 899) found that nivaquine [chloroquine] was able to relieve the reactions which appeared during the course of treatment with sulphone. Its action was not so quick as that of cortisone, but was more prolonged. It can be given along with sulphone and permits larger doses of sulphone at the beginning of treatment.

Many leprosy patients have lesions of the bones of the extremities; LECHAT and CHARDOME (p. 900) show that treatment with DDS may not prevent the progress of mutilations which began before treatment was started, but can prevent mutilations where they have not already begun. Treatment should therefore be started early.

For leprous neuritis HERMANS (p. 900) used chlorpromazine, and for perforating ulcer sodium dehydrocholate with ATS, a product based upon 3% trichloracetic acid and 0·5% salicylic acid.

GOKHALE (p. 774) and also LAVIRON and BEYTOUT (p. 1129) have used intra-arterial injections of ergot alkaloids for the trophic ulcers of leprosy, with some good results.

RANADE *et al.* (p. 775) report some success with epineurectomy for trophic ulcers.

CARAYON and HUET (p. 54) discuss the surgery of nerve leprosy, which has been rendered more successful by the use of sulphones. The paper should be read in full.

FRITSCHI and BRAND (p. 413) discuss reconstruction surgery in the prevention of foot ulceration in leprosy; details should be sought in the original.

Control

ROGERS (p. 1238) traces the progress of leprosy control in the last 40 years. The principles are 4-fold:—1. sample surveys; 2. isolation limited to open lepromatous subjects; 3. voluntary segregation in special villages; 4. repeated examination of contacts. The most important action of the sulphones is their healing of lesions of the nose and throat, and of ulcerating nodes, greatly reducing infectivity. The need for adequate staff and funds is emphasized.

VOGELSANG (p. 1229) gives an account of the disappearance of leprosy from Norway, and the importance of Hansen's discovery in bringing this about.

In a group of Nigerian villages the incidence of leprosy in 1941 was 121 per 1,000, and this fell to 17 in 1955. DAVEY (p. 1230) discusses the reasons for this reduction, giving almost all the credit to the system of segregation villages where everything was done to make life more acceptable than at home. He does not think that cross-immunity with tuberculosis was a factor, public hygiene altered little in the period, and the treatment given in 1941–51 (which was with hydnocarpus oil) contributed little except in indeterminate cases which with this treatment did not become lepromatous.

ROSS (p. 527) gives an account of the control organization in Northern Nigeria, which involves supplying out-patient treatment in clinics within reach of all the patients, and based on existing dispensaries. The results are good.

In a village settlement for leprosy subjects in French West Africa LAVIRON *et al.* (p. 1130) give a combined prophylactic for malaria (pyrimethamine) and leprosy (DDS) to children. The doses are given once each week and the mixture works well for malaria, but it is too early to say what it will do for leprosy.

For South India EKAMBARAM and SHARMA (p. 1239) advocate carefully sited clinics. Leprosy villages (as in Siam) are deprecated because of difficulties over land settlement and the dangers of infection of children.

Rat Leprosy

WALLACE *et al.* (p. 660) have observed limited multiplication of *Myco. lepraemurium* in tissue culture, and a similar finding is reported by REES and WONG (p. 661), who calculate that the generation time of the bacilli is about 13 days, which corresponds with calculations for the organisms *in vivo*. HAWKING (p. 901) has been able to cultivate *Myco. lepraemurium* in tissue

culture, finding that macrophages infected *in vivo* provided the most satisfactory infecting material. He estimates that the number of organisms was doubled at the end of the experiment (52 days). GARBUTT *et al.* (p. 1339) have grown rat leprosy bacilli in tissue cultures of rat fibroblast cells without hydrocortisone.

KÁTÓ (p. 1240) has successfully infected coloured guineapigs with rat leprosy by first stimulating macrophage exudate by intraperitoneal injection of glycogen in saline before intraperitoneal injection of infective material, to provoke phagocytosis and therefore avoid the effect of extracellular fluid, and then by giving an antihistamine daily to the animals.

ENSELME *et al.* (p. 661) report an electrophoretic study of serum proteins of rats with murine leprosy.

NISHIMURA (p. 277) discusses the use of experimental murine leprosy in the study of drugs for the treatment of human leprosy. CHANG (p. 1132) used cycloserine in mouse leprosy; it was moderately effective. He (p. 529) describes the action of 3 isonicotinyl hydrazone compounds found useful in the treatment of murine leprosy.

HIRANO and SUSHIDA (p. 662) show that the addition of a second methoxy radicle to isonicotinyl-4-hydroxybenzal hydrazone increases its already known therapeutic action in leprosy in mice.

From experiments with killed or live rat leprosy bacilli TANIMURA *et al.* (p. 1340) conclude that they, and possibly some other mycobacteria, can confer some degree of immunity.

MALARIA

In this section abstracts are arranged as far as possible in the following order:—Human malaria—*epidemiology, aetiology, transmission, pathology diagnosis, clinical findings, treatment, control;* Animal malaria—*monkeys, other animals, birds.*

DE BUSTAMANTE, F. M. Estado atual do problema da malária. [**Present Position of the Malaria Problem**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1958, Jan., v. 10, No. 1, 79–100. [31 refs.] English summary.

See also p. 1174, GONGORA & MCFIE, **Malnutrition, Malaria and Mortality. The Use of a Simple Questionnaire in an Epidemiological Study.**

FRAGA DE AZEVEDO, J., GÂNDARA, A. F. & FERREIRA, A. P. Contribuição para o conhecimento da endemia malárica na Província de Timor. [**Malaria in Timor**] *Anais Inst. Med. Trop.* Lisbon. 1958, Mar., v. 15, No. 1, 35–52, 1 fig.

The English summary appended to the paper is as follows:—

"The writers observed 3,430 people on Portuguese Timor, of both sexes and different ages. The examinations were carried out during December, January, February and March, and the results are shown on separate tables, where the ages and the altitudes are grouped. Three groups for the age and four areas

for the altitude were considered. They determined the splenic index (I. E.), the average splenic index (I. B. M.), the average enlarged splenic index (I. B. A. M.), the splenometric index (I. Espl.) and the parasite index, total and specific.

" As for the splenic index, they found 46·4% in the more representative group of ages (7 to 14) in the lowest places (0 to 100 meters) and 34·2% in the second zone of altitude (100 to 500 meters).

" The writers found a higher incidence of malaria on the plains near the sea, due principally to the presence of *Anopheles sundaicus*.

" About the parasite rate determinations the writers found the incidence of the *P. falciparum* slightly greater than the *P. vivax*. Next in order comes the *P. malariae* but to a greatly reduced degree."

LAARMAN, J. J. **The Host-Seeking Behaviour of Anopheline Mosquitoes.** *Trop. & Geograph. Med.* Amsterdam. 1958, Dec., v. 10, No. 4, 293–305, 3 figs.

Laboratory-reared *Anopheles maculipennis atroparvus* were tested in their responses to an air stream which had been in contact with various agents, including a rabbit, human exhaled air, a human arm, cattle and rabbit blood. The effect of moist air and carbon dioxide in the air stream was also noted. Mosquito response was assessed by (a) comparison between the number of mosquitoes approaching the " test " and " control " ports of the olfactometer and (b) differences in behaviour at the " test " port; thus, hovering near the port was the predominant reaction when a high concentration of CO_2 was delivered, whereas alighting was seen more frequently when the humidity was raised. The results indicated that smell was a strongly determinative factor in locating the blood supplies and that specific adaptation to a particular host species was possible; thus the odour of rabbit's blood was highly attractive but cow's blood was not. Heat and moisture promote alighting on the host; this thermotactic response to temperature gradient is activated by carbon dioxide. *E. R. Nye*

SENEVET, G., ANDARELLI, L. & BUISSON, R. Une nouvelle station de *Anopheles plumbeus* en Algérie. [**A New Breeding Site of** *Anopheles plumbeus* **in Algeria**] *Arch. Inst. Pasteur d'Algérie.* 1959, June, v. 37, No. 2, 384.

In July 1958 the authors found 3 larvae of *Anopheles plumbeus* in the neighbourhood of Bône, Algeria, 20 km. from the cemetery where they had previously found such larvae in a flower vase [this *Bulletin*, 1956, v. 53, 8]. On the present occasion, the larvae were found in a ditch, together with those of *Theobaldia longiareolata*. This is an unusual breeding place for the arboreal *A. plumbeus*, although it has already been found in ditches in Corsica [*ibid.*, 1926, v. 23 (304)] and in tanks, watercourses and pools in Sardinia [*ibid.*, 1954, v. 51, 1019]. *H. J. O'D. Burke-Gaffney*

TOUMANOFF, C. Étude sur l'anophélisme et le paludisme dans la région du Rio-Nunez (Basse-Guinée). [**Anophelism and Malaria in the Rio-Nunez Region, Lower Guinea**] *Méd. Trop.* Marseilles. 1959, May–June, v. 19, No. 3, 294–311, 3 maps. [10 refs.]

In preparation for the exploitation of bauxite deposits, a survey of anopheles and malaria was carried out in the Rio-Nunez estuary of Lower Guinea. Two

types of terrain were included; brackish water swamp areas close to river or sea affording temporary or permanent breeding places for species adapted to such water, and an elongated raised area near the sea affected by the proximity of the swamps but affording fresh water breeding grounds. The first type has been described previously by TOUMANOFF [this *Bulletin*, 1958, v. 55, 1198]. There are rice fields, mostly dry in the dry season when very few permanent fresh water accumulations exist, but totally inundated in the rains. *Anopheles gambiae* typical race was found, breeding in fresh water but capable of adapting itself to mild salinity, at least up to 1·5 gm. per litre, and invading wide areas during the rains. *A. gambiae* var. *melas* breeds over a wider area and appears to be the major local vector of malaria. All adult *A. gambiae* and *A. melas* females gorged when captured contained human blood. One breeding point was found remote from human habitation, but carriage of adults by favourable winds could not be excluded. In the village houses numerous *A. gambiae* and *A. melas* adults were found at the height of the rains, but none at the end of the dry season. Since breeding was still going on, it is concluded that house spraying would not give effective control in this area. The parasite rate in the small population was up to 71·9% in children and up to 26·2% in adolescents and adults.

The raised area is characterized by elongated depressions which become fresh water swamps of considerable size during the rains. Here *A. gambiae*, *A. obscurus*, *A. coustani* and *A. squamosus* were recovered in seasonal fresh water accumulations. Undoubtedly conditions favour the transmission of malaria. Furthermore, filarial infection was found in *A. gambiae* and the equally widespread *Mansonia uniformis*. *B. B. Waddy*

MAFFI, M. Primo reperto in Somalia di larve di *A. gambiae* parassitate da funghi del genere *Coelomomyces* Keilin, 1921. [**First Report in Somalia of Larvae of *Anopheles gambiae* parasitized by Fungi of the Genus *Coelomomyces***] *Riv. di Malariologia.* 1959, June, v. 38, Nos. 1/3, 71–6, 4 figs. [17 refs.] English summary (2 lines).

SMITH, A. & VAIL, J. W. **Relationship between Salinity and Breeding of *Anopheles gambiae* in North-Eastern Tanganyika.** [Correspondence.] *Nature.* 1959, Apr. 25, v. 183, 1203–4.

The low sporozoite rate of *Anopheles gambiae* in the Pare area of Tanganyika, before residual spraying, prompted the enquiry whether an analogous situation to that in coastal areas existed; in the latter region *A. gambiae* breeding in salt water is known to have a low sporozoite rate. Chloride estimations were carried out on water from various breeding sites in the Pare area, including non-saline, porous, alluvial fans and bordering areas on impermeable soils with high saline contents. In the 42 samples examined the parts of chloride per 100,000 ranged from 2·5 to 170 (0·13% to 8·95% of sea water chloride concentration). Testing of the susceptibility of larvae from eggs obtained from 18 field-caught adults showed that they did not survive saline concentration higher than 34% sea water, not therefore fulfilling RIBBANDS's criterion [this *Bulletin*, 1945, v. 42, 3] for the salt water breeding

A. gambiae. It is concluded that *A. gambiae* in the Pare area is the fresh water type. *E. R. Nye*

PETERS, W. **Albinism in Mosquitoes of the *Anopheles punctulatus* Group.** [Correspondence.] *Australian J. Sci.* 1959, June, v. 21, No. 9, 304–5.

CHARLES, L. J. **Observations on *Anopheles* (*Kerteszia*) *bellator* D. & K. in British Guiana.** *Amer. J. Trop. Med. & Hyg.* 1959, Mar., v. 8, No. 2, Pt. 1, 160–67, 3 figs. [28 refs.]

A new record is given for *Anopheles* (*Kerteszia*) *bellator* in British Guiana. The species was found in the upper reaches of all rivers in the North West District, in the Potaro River, on the Kaieteur escarpment and on the east bank of the Essequibo River. The principal bromeliad plants harbouring larvae of *A. bellator* were *Guzmania capituligera, G. altsonii, Vriesia platynema, V. albiflora, Wittmackia odora* and *Brocchinia micrantha*. Evidence implicating *A. bellator* in malaria transmission in Koriabo (North West District) is presented. The development of hinterland in the North West District, with the growing of cocoa, for instance, could provide suitable conditions for the breeding of *A. bellator* and a warning is given to this effect, based on previous findings in Trinidad. *E. R. Nye*

VELOSO, H. P. O relêvo do solo como fator determinante da distribuição dos anofelíneos na região " bromeliácea-malária " do Brasil. [**Soil Relief as a Factor Determining Distribution of Anophelines in the " Bromeliad-Malaria " Region of Brazil**] *Mem. Inst. Oswaldo Cruz.* 1958, June, v. 56, No. 1, 25–33, 1 map, 3 graphs & 7 charts. [11 refs.] English summary.

The breeding of species of *Anopheles* (*Kerteszia*) in the bases of bromeliads (the so-called Bromeliad-Kerteszia complex) has been investigated in 4 geological zones in the State of Santa Catarina, Brazil. These comprised (i) the continental plains of the basins of two rivers, (ii) quaternary plains of marine sedimentation (Restingas), and (iii) the lower slopes of two mountain ranges.

Larvae of *A.* (*K.*) *cruzii* were present in equal numbers in each region. *A.* (*K.*) *bellator* and *A.* (*K.*) *homunculus* were more restricted in habit. Details are given of their distribution with reference to the topography of the country. *R. J. Wood*

RAY, A. P., SINGH, N., SEN GUPTA, G. P. & MISRA, B. G. **Therapeutic Response to a Newer Antimalarial, 377-C-54.** *J. Indian Med. Ass.* 1959, May 16, v. 32, No. 10, 398–401.

In 1957 BRUCE-CHWATT and CHARLES published the results of a field trial on West African schoolchildren of 377 C 54, a compound belonging to a series of mono- and dihydroxynaphthalenes [this *Bulletin*, 1957, v. 54, 1153]. They concluded that its effect was similar to that of chloroquine but that it was less active against *Plasmodium falciparum* and that its action was less complete.

The observations recorded in the paper now under review were on 124 Indian patients. Of these 22 (13 *P. vivax*, 9 *P. falciparum*) were treated

in hospital with 600 mgm. of the drug in 3 divided doses of 200 mgm. taken at 12-hour intervals. Of the remainder 35 (18 *P. vivax*, 17 *P. falciparum*) received a single dose of 400 mgm. In each of these groups the response of both *P. vivax* and *P. falciparum* was slow, particularly in the case of the latter. However, in 67 cases (*P. vivax* 39, *P. falciparum* 28) treated with a single dose of 600 mgm. in rural areas by domiciliary visits, parasite clearance in both forms of malaria was very similar to that achieved by the 4-aminoquinolines under the same dosage schedule. The drug was well tolerated.

Action against the gametocytes is described as "extremely slow".

G. Covell

SWELLENGREBEL, N. H. **Malaria Eradication.** *Trop. & Geograph. Med.* Amsterdam. 1958, Sept., v. 10, No. 3, 213–20, 1 map.

Professor Swellengrebel reviews the principles and philosophy of malaria eradication, laying emphasis on the radical difference in social impact between control, a collective matter dealing with percentages, and eradication which is progressively more individual in character.

In the industrial mechanisms of British Guiana, from which he draws most of his illustrations, there has been a steady increase in the degree of personal contact between medical and ancillary staff on the one hand and the employee and his family in their home on the other. It has been brought about by a series of changes. The great decrease, or perhaps eradication, of malaria freed hospital and dispensary staff for other activities which gave more varied contact. The overloading of hospitals which paradoxically followed led to the formation of a new medical service; improvement in housing made childbirth in the home more reasonably possible than before and so took medical staff into the house. This degree of home contact, attained by other means and for other ends, assures the virtual certainty that any recrudescent malaria would be observed. It constitutes the fourth, permanent, phase of malaria eradication, the service of maintenance integrated into an organization which is necessary even in the absence of malaria or the risk of it, and so cannot be considered an expense of eradication.

Looking at other mechanisms and recommendations for organization, the author points to the social advantage which is gained by the inclusion of domiciliary visiting services in the later stages of malaria eradication, and to the benefit of training conferred on the staff by participation. The question, often asked, of how staff formerly engaged in malaria eradication can be employed on its achievement needs a total turn of emphasis; one should really enquire how the community can best profit from the experience those workers have gained.

G. Macdonald

GARMS, R., WEYER, F. & REHM, W. F. Jahreszeitliche Schwankungen der Empfindlichkeit gegen DDT bei Freilandpopulationen von *Anopheles atroparvus* und *A. messeae* in Norddeutschland. [**Seasonal Variation in the Susceptibility to DDT of Wild Caught** *Anopheles maculipennis atroparvus* **and** *A. m. messeae* **in North Germany**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1959, Apr., v. 10, No. 1, 48–55. [11 refs.]

The mosquitoes investigated were collected at two localities: at Emden in East Friesland and at Bulkau, near Cuxhaven. At the first locality, repeated

checks showed that the anophelines caught consisted of about 93% *Anopheles maculipennis atroparvus* and 7% *A. m. messeae*, a ratio which has been roughly constant for many years. At Bulkau the mosquitoes have been about 60% *A. m. messeae* and 40% *A. m. atroparvus* in past years, but during the period of the tests the preponderance of *A. m. messeae* was considerably greater.

Tests of susceptibility to DDT were done at different times of the year, by the Busvine/Nash method. Usually the mosquitoes were tested within a few hours of capture, but a few tests were done after keeping them for several days in a laboratory (at 26°C. and 80% RH). The LC50 calculated at different times varied from 2·5% to 1·5% for *A. m. atroparvus,* being highest in autumn and lowest during hibernation and soon afterwards. Fewer data were obtained with *A. m. messeae*, which were throughout more susceptible; but these mosquitoes, too, showed increased resistance in September.

The reduced susceptibility at the onset of hibernation agrees with the findings of previous investigators [De Zulueta *et al.*, this *Bulletin,* 1957, v. 54, 1052; Duport *et al.*, *ibid.*, 1959, v. 56, 593] but is not so pronounced. The present authors ascribe the reduced susceptibility at onset of hibernation to increased fat body and changed metabolism associated with gonotrophic dissociation. [This must be the only explanation since they have informed the abstracter that all tests were done at 25°C., whereas the tests of earlier authors were done at room temperature. This introduces another variable since the summer temperatures were, in different cases, 4°, 8° and 10°C. higher than autumn ones. The higher temperature would increase activity and probably result in the mosquitoes picking up a larger dose. Hence the bigger differences noted by De Zulueta *et al.* and Duport *et al.*].

Additional experiments were done on *A. m. atroparvus* and *A. stephensi* from laboratory cultures, to investigate effects of physiological state on susceptibility. Unfed mosquitoes (both wild and colony reared) were most susceptible; they became more resistant after a meal. Indeed, with regular feeding the females went through a cycle of increasing and decreasing susceptibility, as described by Hadaway and Barlow for *Aëdes aegypti* and *Anopheles stephensi* [*ibid.*, 1957, v. 54, 534]. *J. R. Busvine*

Voelckel, J. & Mouchet, J. Quelques aspects et résultats de la désinsectisation systématique en milieu urbain tropical. [**Some Aspects and Results of Insecticide Spraying in a Tropical Urban Area**] *Méd. Trop.* Marseilles. 1959, May–June, v. 19, No. 3, 266–93, 3 plans. [15 refs.]

House-spraying with residual insecticides has been practised at Douala, French Equatorial Africa, since 1951. Nevertheless, in 1955 there was a sharp rise in malaria incidence. It was decided that the antimosquito campaign should be raised to the highest possible level of efficiency, in particular to achieve not less than 95% coverage of houses with residual insecticide. DDT wettable powder, or dieldrin in modern hardwalled houses, was used for house-spraying; walls were sprayed to a height of 2 metres; the backs and undersurfaces of furniture were sprayed, and residents were warned in advance of spraying dates in order to clear their walls of obstructions. Refusal of entry was more frequent in high class areas, but was largely overcome during the campaign. Each spraying programme took nearly 6 months, and two were completed in the year. In addition periodical fogging, with a DDT-dieldrin

mixed solution in a TIFA machine, was carried out with the intention of destroying exophilic mosquitoes; drains etc. were treated with BHC or malathion preparations, and careful attention was paid to small natural and man-made breeding places. Control of the campaign was improved by decentralizing supervision into the charge of sectional health authorities. Daily and monthly written returns of work done were rendered, and in addition each section chief gave a verbal progress report at a weekly meeting.

At the beginning of the intensive campaign, *Anopheles gambiae* was the only anopheline found inside houses, at a mean density of 0·92 per house (sporozoite rate 11·2%). *A. funestus*, abundant in 1953, had disappeared, no doubt owing to previous spraying. Larval forms of *A. coustani* and *A. nili* were found during a survey of breeding places. When the entomological survey was repeated a year later, no anopheline was found in any house, and only 4 breeding places contained larvae of *A. gambiae*. No *A. nili* was found, but *A. coustani* was apparently unaffected. *Culex pipiens fatigans* was abundant and apparently little affected by the campaign. *Aëdes aegypti*, an exophilic mosquito in the Southern Cameroons, seemed to have been reduced in density by the general antilarval campaign, but results were not assessed with rigorous accuracy. As side effects of the spraying campaign, *Tunga penetrans* virtually disappeared from Douala, and no fleas were found on rats after the first few months. Between 1955 and 1957 deaths in hospital from malaria dropped from 27 to 1; infection rates among children attending the child welfare clinics dropped to nil by October 1957, this result being considered particularly significant.

The success of the campaign in ridding Douala of *A. gambiae* must be attributed mainly to residual spraying, other methods being adjuvants. Mouchet and Gariou [this *Bulletin*, 1958, v. 55, 245] achieved equally good results at Yaoundé by spraying alone. No complacency should be engendered by present success.

[An important paper, containing detail that cannot be included in the abstract.] *B. B. Waddy*

Dowling, M. A. C. & Hughes, R. D. **Malaria Control by Residual Spraying reinforced by Short-Term Chemoprophylaxis.** *J. Roy. Army Med. Corps.* 1959, Apr., v. 105, No. 2, 61–70, 3 figs.

Pulau Tioman is a small island off the east coast of Malaya, 14 miles long and with about 1,000 inhabitants. Survey in June 1955 showed spleen and parasite rates respectively in children aged 5 to 9 years of 68% and 60%, and *Plasmodium vivax* constituted 83% of the parasites found, though perhaps this was the abnormal result of a recent epidemic. No vector anophelines were found in a brief search, but control measures were instituted on general principles:—the immediate application of dieldrin as a smoke in selected places, residual dieldrin at 50 mgm. per sq. ft. inside houses, and medication of the population with one dose of chloroquine (0·6 gm. for adults) and 6 weekly doses of proguanil (0·3 gm. for adults). Resurvey in 1956 showed spleen and parasite rates of 29·6% and 1·8% in the 5 to 9 year age-group. This success leads the author to conclude that a combination of therapy with imagicidal attack might hasten eradication. *G. Macdonald*

PETERS, W. & STANDFAST, H. A. **The Susceptibility of Mosquitoes of the *Anopheles punctulatus* Group to Chlorinated Hydrocarbon Insecticides.** Reprinted from *Australian J. Sci.* 1958, Mar.–Apr., v. 20, No. 7, 218–19.

An account is given of spray trials with dieldrin against malaria vectors of the *Anopheles punctulatus* group (*A. punctulatus*, *A. farauti* and *A. koliensis*) in the Sepik District of the Territory of Papua, New Guinea.

A coastal strip extending 3 miles inland and about 20 miles wide was treated by residual house-spraying with a 50% dieldrin wettable powder at the rate of 0·5 gm./m^2 between May and June 1957. The densities of all mosquitoes dropped dramatically but after 4 months anophelines began to return. By the end of 6 months the numbers of house-resting anophelines had returned almost to their former levels.

Tests by a modified Busvine-Nash method indicated that no resistance had developed either to dieldrin or to DDT. All 3 species were highly susceptible to both insecticides. The order of susceptibility was: *A. punctulatus* (the most susceptible), *A. farauti* and *A. koliensis*.

It is concluded that, for effective anopheline control, house-spraying must be done at least once every 6 months. *R. J. Wood*

ACOSTA, M. Niveles basicos de susceptibilidad del *Anopheles pseudopunctipennis* al DDT y al Dieldrin en la region occidental del Peru. [**Basic Levels of Susceptibility of *Anopheles pseudopunctipennis* to DDT and to Dieldrin in the Western Region of Peru**] *Rev. Med. Exper.* Lima. 1958, Dec., v. 12, Nos. 1/2, 99–106, 1 map. English summary.

The English summary appended to the paper is as follows:—

"Using techniques recommended by WHO the author conducted studies from December 1957 to May 1958 on the susceptibility of *Anopheles pseudopunctipennis* to DDT and Dieldrin insecticides. The mosquitoes were captured along the coastal region of Peru, where during the past few years, extensive spraying has been done with chlorinated carbon insecticides.

"Results showed that the LD_{50} for mosquitoes for DDT was between 0·38 to 0·92 percent, and for Dieldrin between 0·13 and 0·26 percent respectively.

"These values are within the limits of normal susceptibility of non-resistant strains of *A. pseudopunctipennis*."

SOEIRO, A. A campanha anti-sezonática no vale do Limpopo. [**The Anti-malarial Campaign in the Limpopo Valley**] *Anais Inst. Med. Trop.* Lisbon. 1957, Sept.–Dec., v. 14, Nos. 3/4, 389–406, 1 fig.

The English summary appended to the paper is as follows:—

"The author explains that in an agricultural region highly hyperendemic where a non-immune population of Europeans was installed, after 3 years of treatment, although he could not interrupt completely the transmission of the disease was able to control it. He established a semi-urban hypoendemic and salubrious area, in a rural region which is considered today as mesoendemic, the salubrity of which is very satisfactory."

SERGENT, Ed. Réflexions sur l'épidémiologie et l'immunologie du paludisme. [**Reflexions on the Epidemiology and Immunology of Malaria**] *Arch. Inst. Pasteur d'Algérie*. 1959, Mar., v. 37, No. 1, 1–52. [74 refs.]

The author summarizes his experiences since the beginning of the century on the general subject of the attacking power of malaria parasites *vis à vis* the resistance of the host. The paper is based on 74 studies made by himself and collaborators at the Pasteur Institute of Algeria, chiefly on *Plasmodium relictum* and *P. berghei*, and in the case of the former, the reaction of the mosquito host is considered just as much as the vertebrate. The human parasites (with the exception of *P. ovale*, which is said to be absent from Algeria) are also discussed indirectly.

The paper is divided into two main divisions—the first deals with primary infections and innate resistance, the second with re-infections and acquired resistance—and the original observations have been abstracted in this *Bulletin*, almost from the first volume. Perhaps the most interesting chapters relate to the behaviour of the *Plasmodium* in the mosquito, either as a first or later invader, and it is noteworthy that the invertebrate host fails to react in any way to the presence of the parasite; interesting observations are reported on unusual ways of introducing sporozoites or merozoites to the vertebrate. The course of the infection in the vertebrate is described in some detail, always from the point of view of the reaction between host and parasite. The observations on the failure of quinine to prevent infection if given during the incubation period were recognized by the author as being highly suggestive of an exo-erythrocytic phase, and are here re-described. Interesting data are given on degenerate forms of the parasite, the loss of ability to produce gametocytes, occultation in presence of other organisms etc. The subject of premunition is clearly exposed, and it is to be noted that in malaria, premunition is not strictly confined to strains but exists in some degree between related species (*e.g. P. relictum* and *P. cathemerium*).

The author concludes with the recommendation of Pasteur of not insisting upon an absolute, but being content with a relative degree of immunity.

P. C. C. Garnham

TRAGER, W. **The Enhanced Folic and Folinic Acid Contents of Erythrocytes infected with Malaria Parasites.** *Exper. Parasit.* New York. 1959, June, v. 8, No. 3, 265–73, 1 fig. [22 refs.]

In an earlier report TRAGER (*Science*, 1957, v. 126, 1236) indicated the enhanced folic and folinic acid content of red cells infected with malaria parasites. The evidence available suggests that folic acid and related compounds are of importance in the metabolism of these parasites [this *Bulletin*, 1949, v. 46, 1124; 1950, v. 47, 214; 1959, v. 56, 278]. For this reason the author has made a comparison of the folic and folinic acid content of normal red cells, infected cells and of the free parasites. The avian parasite *Plasmodium lophurae* maintained in ducks was used. Folic and folinic acids were assayed microbiologically, after dialysis of a haemolysed sample of the red cells through a "cellophane" sac into 0·1 M buffer solution. The apparatus used is clearly depicted. The preparation of free parasites was obtained by suitable antiserum and removal of red-cell nuclei by deoxyribonuclease, followed by

dialysis at 40° as above. The actual method of assay of folic acid was that described by TOENNIES *et al.* (*J. Biol. Chem.*, 1953, v. 200, 23), usually with *Lactobacillus casei*, growth being measured by titration of the acid formed over a period of 3 days at 37°C. Folinic acid was assayed in a medium to which folic acid had been added with *Leuconostoc citrovorum* as the test organism. The standard for comparison consisted of folic acid and leucovorin in known amounts previously dialysed as above. The assays are stated to be accurate to within approximately 15%. An increase approximately 20–50-fold in folic acid and of 5–20-fold in folinic acid occurred in infected red cells of 2-month-old ducks compared with normal ducks of the same age. The malaria parasite thus appears to affect markedly the metabolism of the host cell. There was relatively little folic or folinic acid in the parasite. *J. D. Fulton*

TRYPANOSOMIASIS

In this section abstracts are arranged as far as possible in the following order:—African—*human, animal;* American—*Chagas's disease and other trypanosome infections. In each form the following order is followed:*—*epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control.*

MOÇAMBIQUE. Missão de combate às tripanossomíases. Relatório annual de 1956 [DE ANDRADE SILVA, M. A.]. [**Annual Report for 1956 of the Trypanosomiasis Commission**] 106 pp., 2 charts (1 folding), 3 maps (2 coloured folding) & 11 figs. 1959. Lourenço Marques: Imprensa Nacional de Moçambique.

The first section of the report deals with the density and distribution of *Glossina morsitans, G. brevipalpis, G. pallidipes* and *G. austeni,* which are discussed for the regions Cabo Delgado, Lalaua, Mogovolas, Alto Molócuè, Lugela, Derre, Manica, Mabote, Massangena and Vilanculos in Portuguese East Africa.

The annual return of new cases of sleeping sickness for 1956 was 127, the lowest figure since 1942, and was due to the low return from Mocimboa da Praia, the major endemic region, after a chemoprophylactic campaign. Of the 127 cases, 30 came from the district of Tete, 8 from Mozambique and 89 from Cabo Delgado. The incidence per 1,000 persons examined was 0·17 and the mortality of hospital cases of sleeping sickness was 8%.

In the sections on control, measures against the disease included blood examinations of workers on sisal plantations and others exposed to infection and the use of pentamidine injections for these persons, both African and European. Fly control measures included clearing, fly checks on transport and indiscriminate game destruction. The question of repopulation of cleared areas and water supply was also discussed.

In the treatment of domestic cattle for nagana, 57,711 animals were dealt with in 1956, chiefly with dimidium bromide and also antrycide methylsulphate.

Other data given include statistics of laboratory examinations carried out at the various sectoral laboratories and movement of patients in and out of hospital, and data on treatments employed. *E. R. Nye*

WIJERS, D. J. B. **Polymorphism in** *Trypanosoma gambiense* **and** *Trypanosoma rhodesiense,* **and the Significance of the Intermediate Forms.** *Ann. Trop. Med. & Parasit.* 1959, Apr., v. 53, No. 1, 59–68, 7 figs.

There is considerable difference of opinion regarding the nature of polymorphism in trypanosomes of the *brucei* group, some authors regarding the three dominant forms (slender, intermediate and stumpy) as distinct entities, others believing that one stage is transformed into another by division or by syngamy, while others again are of the opinion that they were produced under the influence of changes in the environment or of the immune reactions of the host.

In order to solve this problem, the author studied the course of infection in monkeys and rats infected with *Trypanosoma gambiense* and *T. rhodesiense*, by making daily counts of the numbers of different forms present and correlating the findings with parasitaemia.

It was found that the morphology of the trypanosomes depended upon the degree of parasitaemia: during a rise the proportion of slender forms was highest, while during a decrease stumpy forms were predominant. As regards the intermediate forms, a study of the phase of infection when their numbers were highest indicated that they are transitional forms, produced by slender forms as they shrink to become stumpy forms, and when the latter grow to become slender forms again. This correlation between polymorphism and parasitaemia is illustrated by a series of graphs, while the actual transformation of slender forms into stumpy forms was also observed *in vitro*.

It is suggested that these morphological changes take place as the result of trypanosomes adapting themselves to alterations in the host environment.

C. A. Hoare

FULTON, J. D. & SPOONER, D. F. **Terminal Respiration in certain Mammalian Trypanosomes.** *Exper. Parasit.* New York. 1959, Apr., v. 8, No. 2, 137–62, 4 figs. [43 refs.]

This paper is not concerned with the trypanosomes' last gasp, as the title suggests, but with the final stage of oxidative metabolism. VON BRAND and TOBIE (*J. Cellular Comp. Physiol.*, 1948, 31, 49) and other workers have shown that a species difference exists between trypanosomes in sensitivity to cyanide, suggesting that some species absorb oxygen by means of a cytochrome system while others do not.

This paper shows by a number of specific tests that a cytochrome system is absent in the blood forms of *T. vivax, T. congolense* and the *brucei* group, but is present in those of *T. lewisi* and probably in *T. cruzi*. It is present, however, in the culture forms of *T. gambiense*, as well as those of *T. cruzi, T. lewisi* and in *Strigomonas oncopelti*.

The authors point out that *T. rhodesiense* respires by the normal Emden-Myerhof-Parnas cycle [this *Bulletin*, 1957, v. 54, 1163] ending in pyruvic acid, thereby reducing diphosphopyridine nucleotide (DPN). This is oxidized by molecular oxygen with a high respiratory quotient without the mediation of a cytochrome system, flavoproteins, or peroxidases. An oxidase probably exists, but they were unable to isolate it.

[This most interesting but technical paper should be referred to in the original.]

W. E. Ormerod

JANZ, G. J., DE CARVALHO, A. M. & MADEIRA, O. G. Novos dados sobre a mancha de *Glossina morsitans* do Alto Zambeze (Moxico-Angola). [**Recent Information on a Focus of** *G. morsitans* **in the Upper Zambesi Area of Angola**] *Anais Inst. Med. Trop.* Lisbon. 1957, Sept.–Dec., v. 14, Nos. 3/4, 383–7, 1 map.

The English summary appended to the paper is as follows:—

"The authors described the result of a survey, made by the 'Missão de Prospecção de Endemias' in Angola, in the region of the 'Alto Zambeze' (Moxico, Angola) where before had been already shown the presence of *Glossina morsitans*.

"It seems to be concluded by the observations made, that the mentioned spot has expanded in the last years to the West."

RICHET, P., LOTTE, M. & FOUCHER, G. Resultats des traitements de la trypanosomiase humaine a *T. gambiense* par le Mel B ou l'arsobal dans le secteur special No 43 à Natitingou (Nord Dahomey). [**Treatment of** *Trypanosoma gambiense* **Infection with Mel B in a Special Sector in Dahomey**] *Méd. Trop.* Marseilles. 1959, May–June, v. 19, No. 3, 253–65.

Mel B was introduced into North Dahomey in 1948; in the past 10 years it has been used for the treatment of 795 patients suffering from trypanosomiasis. This paper is an analysis of the results of that treatment.

The types of disease from which the patients were suffering are classified as follows:—(1) untreated first stage cases; (2) untreated second stage cases; (3) second stage cases previously treated with other drugs, but still with parasites in the cerebrospinal fluid [CSF]; (4) advanced second stage cases with abnormal CSF from which parasites could no longer be recovered.

All the patients in the first group (181) remained under adequate observation; 3 (1·65%) died as a result of toxicity of the drug; 9 died of intercurrent infections; but, excluding these latter, 97% of those treated responded well to treatment and the end result was satisfactory over the varying periods of observation. 160 (88%), as a result of prolonged observation, are considered to have been cured radically.

Of those in the second group (391) 3 vanished immediately after treatment; 15 (3·83%) died from the toxic effect of the drug; 28 have died of intercurrent infections; and 27 have died of trypanosomiasis. Excluding those dying of intercurrent infection (but showing no sign of continuing trypanosomiasis), in 82% the immediate and end result over varying periods of observation was good. 252 (64·5%) were radically cured, as judged by adequate observation.

Of the third group (95) 3 vanished; 1 (1·05%) died as a direct result of the treatment; 6 have died of intercurrent infections; and 20 have died of trypanosomiasis. A good result may be assumed in 68·5% and radical cure was established in 58 (61%).

Of the fourth group (128) 2 vanished; none died as a consequence of the treatment; 3 have died of intercurrent infections; and 24 have died of trypanosomiasis. So in 69% a good result may be assumed, and cure was established in 69 (54%).

The authors analyse their data in some detail and give examples of cases

illustrating successful (radically curative) treatment with Mel B after unsuccessful courses of treatments with other drugs, which included the arsenicals, diamidines and suramin.

They consider that the results obtained with Mel B in the treatment of trypanosomiasis at all stages in North Dahomey have been remarkable. They recognize that in other areas the results may not be so consistently good, and they mention a number of factors (individual, nutritional, local and epidemiological) which may influence the response of the disease to treatment with this drug in other areas.

Fatalities due to the drug totalled 19 (2·38%); all occurred before 1952; there have been none among the 148 patients treated since then. This fall in fatality they ascribe to more rigorous precautions in the use of Mel B and modifications in the treatment régimes used. The drug, properly handled, is relatively innocuous. The rules for safety that they recommend are treatment of first stage cases with the diamidines alone; not Mel B. This drug should not be used in the very young; in those in very poor general condition; and in those with psychic changes. It should only be given to those with advanced disease, or with a diffuse parasitic infection. BAL should always be available in emergency for the treatment of toxicity due to the Mel B. As a general rule Mel B treatment should be preceded by a course of tryparsamide treatment; this latter opinion is not by any means generally accepted, and may well be criticized. Nevertheless, in this series of cases the fatal accidents predominantly occurred in those who had not had previous treatment for the disease. *A. R. D. Adams*

Friedheim, E. A. H. & De Jongh, R. T. **Mel W, a New Trypanosomicidal Agent derived from Mel B.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1959, May, v. 53, No. 3, 262–9.

Arsobal (Mel B; melarsen oxide BAL) is insoluble in water; it therefore is given intravenously in solution in propylene glycol. Its water-lipid coefficient favours the lipid phase, thus enhancing its affinity for the central nervous system and its toxic action on it.

A water-soluble derivative of arsobal has now been synthesized; it is named Mel W. This can be given intramuscularly. In white mice it has proved equal to arsobal as a trypanocide; when given intraperitoneally it proved only half as toxic to them.

8 patients in Liberia, ranging in age from 8 to 50 years and suffering from *Trypanosoma gambiense* infections, were treated with Mel W. Of these 2 patients were first-stage cases; 3 were second-stage cases, fairly advanced and somnolent; another 2 were later second-stage cases in semi-coma; and the last was in a very advanced state with gross mental and nervous disturbance. Parasites were recovered from all but the last patient; the cerebrospinal fluid [CSF] of this patient was markedly and typically abnormal. Details of the condition of the patients, the relevant findings, and the treatment are set out in tables, as are also the immediate and later results of treatment. The latter took the form of intramuscular or subcutaneous injections of a 5% solution of Mel W in saline or glucose solution daily for 4 days, which was repeated after an interval of a week. The daily dosage used ranged from 1·0 to 5·0 mgm./kgm. of body weight.

Significant findings following treatment were the disappearance of parasites from the blood and gland juices within 2 hours of the first injection; the disappearance of parasites from, and a marked fall in the cell count in, the CSF within a couple of weeks; a slower fall in the CSF protein content, which became marked only after 2 months; and amelioration of the clinical picture which was progressive and significant.

No evidence of severe toxicity attended the use of the drug; but the very advanced stage patient was severely prostrated after his first 2 injections. This is often the case in those treated with arsobal; it confirms the view that in advanced cases the initial dosage with these drugs should be small; as the condition improves fuller dosage can be introduced.

On this limited study Mel W shows significant improvement on arsobal; the most satisfactory schemes of dosage with it for various types of case, and for tryparsamide-fast cases, must await fuller investigation and more prolonged observation of those treated with the drug. *A. R. D. Adams*

TRINCAO, C., DA GRACA, Maria M., DA FONSECA, P. & NOGUEIRA, A. R. Action de l'amphomycine sur l'infection expérimentale de la souris par *Trypanosoma rhodesiense*. [**Action of Amphomycin on Experimental Infections with** *T. rhodesiense* **in Mice**] *Bull. Soc. Path. Exot.* 1958, Nov.–Dec., v. 51, No. 6, 893–6

Amphomycin was first isolated in 1953 and its effect on trypanosome infections was studied. It was inactive against *Trypanosoma cruzi* but had some effect against *T. rhodesiense* and *T. gambiense* [this *Bulletin*, 1957, v. 54, 542]. The authors have now studied its effect on a virulent strain of *T. rhodesiense* in 190 mice infected and also treated by the intraperitoneal route. Treatment was started on the day of infection with doses ranging from 20 to 125 mgm. per kgm., and up to 10 doses were given. After 48 hours the mouse blood was examined for trypanosomes and the examination was continued for 10 weeks in surviving animals.

The results obtained depended on dosage of drug and frequency of treatment. 100% of cures were obtained when 125 mgm./kgm. were given on 5 consecutive days, and results with other dosages are summarized in tables. The drug had no prophylactic properties and immunity did not develop in the animals which survived. *J. D. Fulton*

DA SILVA, J. M. Subsídos para o estudo das infestações tripanosómicas mistas de alguns animais domésticos. [**Contributions to the Study of Mixed Trypanosome Infections of Domestic Animals**] *Anais Inst. Med. Trop.* Lisbon. 1957, Sept.–Dec., v. 14, Nos. 3/4, 483–502. English summary.

D'ALESANDRO, P. A. **Electrophoretic and Ultra-centrifugal Studies of Antibodies to** *Trypanosoma lewisi*. *J. Infect. Dis.* 1959, July–Aug., v. 105, No. 1, 76–95, 7 figs. [29 refs.]

RAMOS, A. DA S. & LIMA, Helena M. DE A. Casos humanos de moléstia de Chagas parasitologicamente comprovados no Estado de São Paulo (Brasil). [**Human Cases of Chagas's Disease parasitologically confirmed in Sao Paulo, Brazil**] *Folia Clin. et Biol.* S. Paulo. 1956, July–Dec., v. 26, Nos. 1/6, 3–8, 1 map. [27 refs.]

The English summary appended to the paper is as follows:—

"The authors are making a revision in the works already accomplished in the State of São Paulo on the detection of the *Trypanosoma cruzi* by direct examination, xenodiagnosis and inoculation.

"They present a list of counties where existence of the disease was evidenced by parasitologic examinations."

CORREA, R. R. & CARVALHO, P. J. *Panstrongylus diasi* Pinto & Lent, 1946. Sua presença no Estado de São Paulo (Hemiptera, Reduviidae). [**Presence of *Panstrongylus diasi* in Sao Paulo, Brazil**] *Folia Clin. et Biol.* S. Paulo. 1956, July–Dec., v. 26, Nos. 1/6, 79–84, 3 figs. English summary (3 lines).

KNIERIM, Feliza. Resultados obtenidos con la reacción de fijación del complemento según el 50% de hemólisis en el diagnóstico de la enfermedad de Chagas. [**Results obtained with the 50% End-Point Complement-Fixation Test in the Diagnosis of Chagas's Disease**] *Bol. Chileno de Parasit.* 1959, Jan.–Mar., v. 14, No. 1, 5–6. [11 refs.]

The English summary appended to the paper is as follows:—

"The 50% end point hemolysis technique for the complement fixation test was performed in sera specimens of 116 individuals with negative xenodiagnosis, although suspected of Chagas' disease, and 29 confirmed cases by xenodiagnosis. The serological reaction was positive in 90% of the confirmed cases, while in 7% was doubtful, the rest being negative. 36% of the suspected individuals have also a posititve test, in contrast to 2% of positive reactions in a group of 100 apparently healthy adults. The discrepancy between the relatively high percentage of positive serological reactions in the suspected cases and the negative xenodiagnosis may be explained on the basis of the difficulty of obtaining positive xenodiagnosis in chronic cases of Chagas' disease."

BRENER, Z. & PELLEGRINO, J. Observações sôbre a ação do 2-acetamido-5-nitrotiazol sôbre a infecção experimental do camundongo pelo *Trypanosoma cruzi*. [**The Action of 2-acetamido-5-Nitrothiazole on Experimental *T. cruzi* Infection in Mice**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1958, July, v. 10, No. 3, 327–30, 2 figs.

The English summary appended to the paper is as follows:—

"The therapeutic activity of 2-acetamido-5-nitrothiazole was studied in mice experimentally infected with *Trypanosoma cruzi*. When given orally (200 mg./kg. twice a day) a definite reduction of parasitemia and a decrease of rate mortality was observed. This action was more marked when the compound was administered by the drug-diet method (0·5% dosage). The drug has no activity upon tissue forms of the parasite and does not show protective action."

LEISHMANIASIS

In this section abstracts are arranged as far as possible in the following order:—visceral, cutaneous, muco-cutaneous.

HEISCH, R. B., GRAINGER, W. E. & HARVEY, A. E. C. **The Isolation of a *Leishmania* from Gerbils.** *J. Trop. Med. & Hyg.* 1959, July, v. 62, No. 7, 158–9, 1 map.

The senior author had already shown some evidence that gerbils were reservoirs of kala azar in the Kitui district of Kenya [this *Bulletin*, 1955, v. 52, 520].

There have been cases of kala azar in man in the Kerio Valley which is an offshoot of the Rift Valley. Some 10 miles north of a camp in Rimo in the Kerio Valley where a human case occurred 10 years ago, there are numerous gerbils [*Tatera nigricauda*]. The authors examined 251 gerbils between 1956 and 1958 and although the animals looked healthy and their spleen smears were negative, leishmaniae were isolated on 3 occasions when emulsified spleens were inoculated into hamsters.

The authors speculate on whether gerbils in the Kerio Valley can infect sandflies or whether they develop only " blind alley " infections.

The *Leishmania* of gerbils is morphologically similar to *L. donovani* and causes heavy infection in hamsters. It caused localized nodules containing leishmaniae when inoculated into the skin of man but these faded in a few weeks, without visceral involvement [*ibid.*, 1959, v. 56, 928]. Patients challenged thereafter with *L. donovani* proved immune, so that it seemed unlikely that the gerbil strain was *L. tropica*. Its exact status has therefore still to be determined. *H. J. O'D. Burke-Gaffney*

FEVERS OF THE TYPHUS GROUP

In this section abstracts are arranged as far as possible in the following order:—general; louse-borne typhus, flea-borne typhus, mite-borne typhus; rickettsialpox; tick-borne typhus; Q fever, other rickettsial diseases.

LEGKODIMOVA, K. V. **Some Information regarding Exanthematic Typhus in the Primor'e.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 11, 1783–5, 1 fig. [Translated from Russian.]

The results of agglutination and complement-fixation tests with *Rickettsia prowazeki* and *R. mooseri* antigens indicated that patients with typhus fever seen in the Primor'e region during the period 1954–6 were infected with *R. prowazeki*. Retrospective investigation of sera from patients seen before 1954 who had been diagnosed on clinical and epidemiological grounds as having murine typhus suggested that *R. prowazeki* had also been responsible for these illnesses. Recurrent typhus is common (" recorded at 40·7% "), but louse infestation in both primary and recurrent cases is said to be negligible. Adults were chiefly affected, 63% of patients being women. Seasonal variations in

incidence were not observed. The disease is mild, although fever persisting for 15 days or more occurred in 73% of primary infections. No fatal cases have been seen. A roseolar polymorphic exanthem occurred in 80·8% of patients and a severe haemorrhagic exanthem in 4·5%. The Weil-Felix test was negative in 42% of cases; the complement-fixation test was negative in 9% of primary cases and in 1% of recurrent cases.

"Further investigations are necessary for the final clarification of this problem."

R. S. F. Hennessey

SOMOVA, A. G., GERASIUK, L. G. & DEDUSENKO, A. I. **The Serological Diagnosis and Epidemiology of Typhus.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 11, 1786–9. [Translated from Russian.]

The English version of this paper opens with these words: "The complete elimination of typhus in the U.S.S.R. is complicated by certain characteristics of this disease which have developed in recent years (the presence of atypical and abortive forms)". The authors then go on to consider the results of serological investigations of a series of patients with a clinical diagnosis of typhus. The sera were examined for the Weil-Felix reaction, *Rickettsia prowazeki* agglutinins and *R. prowazeki* complement-fixing antibodies by the usual techniques, but it would appear in the majority of cases that only a single specimen of serum was examined. In a few cases serial tests were done. The results reported here show that the complement-fixation test was the most valuable, followed by the rickettsial agglutination test but with the Weil-Felix reaction not far behind. Maximum titres in all cases seemed to develop in the second week of the disease; antibodies were tending to fall by the third week.

Epidemiological studies failed to connect any of the cases with each other or known cases of typhus. The question of the influence of lice was also eliminated. The most important fact brought out by the enquiries made was that well over half of the patients involved had had a previous attack of typhus or were known to have been exposed to the risk of infection.

[This paper is of very considerable interest to the abstracter. The authors appear to be well aware that the majority of the cases, at least, are examples of the recrudescence of epidemic typhus, yet there is no text reference to the original observations of BRILL (*N. Y. Med. J.*, 1898, v. 67, 48, 77), or any later communication on the Brill-Zinsser disease. There is no terminal list of references in the English version.] This is the first account, as far as is known, of the recognition of Brill-Zinsser disease in the U.S.S.R. and the fact that out of a total of 271 febrile patients in infectious diseases hospitals who were examined, 61 were diagnosed as having typhus (the majority were classified as having the recurrent form) suggests that recrudescence of the original infection is by no means uncommon in that country. Of 170 patients suffering from diseases other than typhus only 5 were found to have specific antibodies against *R. prowazeki*. Details of the medical history of these patients are not given but it may be of interest to recall that in a recent survey of 318 unselected healthy Polish born subjects [LAWY *et al.*, this *Bulletin*, 1959, v. 56, 25] 22%, irrespective of their medical history, had specific typhus antibodies in their sera.

H. J. Bensted

MISKOV, D. [**Contribution to Epidemiological Investigations in Voïvodina**] *Med. Pregled.* Novi Sad. 1958, v. 11, No. 5, 258–62. [16 refs.] [In Serbian.]

The English summary appended to the paper is as follows:—

"The author describes 6 cases with Brill-Zinsser's disease in the province Banat among immigrants from Bosnia. The cases appeared following some febrile disease and the average duration of the illness amounted to 8–10 days. The clinical picture was that of meningitis in one case, of typhoid fever in two cases and of grippe in three cases. Relapse appeared after 13·5 years on an average."

AKAISHI, S. [**A Death caused by Typhus Vaccination**] *Hirosaki Med. J.* 1959, Mar. 25, v. 10, No. 2, 227–32. [In Japanese.] English summary *33–*35.

A case in a child of 13 who died 10 minutes after typhus vaccination. She was allergic to eggs.

MISSIRLIU, C., MISSIRLIU, Marie F. & ETTELDORF, J. N. **Rocky Mountain Spotted Fever in Children.** *J. Pediatrics.* St. Louis. 1958, Sept., v. 53, No. 3, 303–10, 2 figs. [13 refs.]

20 cases of Rocky Mountain spotted fever in children, aged from 3 to 13, seen during a 12-year period in Memphis, Tennessee, are described. A petechial and morbilliform rash occurring about the 4th day of the fever was the most striking clinical feature. It appeared on the extremities and spread to the trunk, involving the palms and soles. 8 patients had oedema of the face and eyelids. Intense myalgia and malaise were constant. Rising titres of agglutinins to *Proteus OX19* were demonstrated in 17 patients. In the remaining 3 cases no agglutinins were found. The rickettsial complement-fixation test was positive in the 8 cases in which it was done.

The diagnosis was not considered difficult, but in some instances it was thought necessary to exclude the possibility of meningoccocal septicaemia by examining the cerebrospinal fluid and by blood culture. Those patients treated with the tetracyclines or with chloramphenicol responded satisfactorily.

The authors stress the importance of "supportive therapy" in children, that is "the correction of electrolyte imbalance by fluid administration and the replacement of plasma lost to the tissues". *D. R. Seaton*

LUTYNSKI, R. & RAGINIS, Zofia. Badania ludzi w województwie krakowskim w kierunku zakażenia *R. burneti.* [**Examinations of Human Beings in the Province of Cracow for Infection with** *R. burneti*] *Przegląd Epidemiol.* Warsaw. 1959, v. 13, No. 2, 185–8. [12 refs.]

The English summary appended to the paper is as follows:—

"The authors give the results of serological examinations carried out in order to discover any possible undiagnosed cases of Q fever amongst those living in the Cracow province. The complement fixation test was applied, using the antigen of *R. burneti* of the Henzerling strain.

"Among those especially exposed to infection (workers in slaughter-houses, tanneries, agriculture, health inspectors of hunting grounds, and those engaged in pasturing sheep), 1461 persons were examined, as well as some patients, chiefly those suffering from atypical pneumonia.

"Two positive results of the complement fixation test were obtained, confirmed by repeated serological tests and characteristic data from the case-histories, in which both cases (a worker at a wool-collection centre and a shepherd) stated that a year previously they had influenza with symptoms characteristic of Q fever (headache, epistaxis, maintained fever, cough, pneumonia).

"The authors presume that these cases were Q discovered *ex post*, and conclude that the infection might most probably have been caused by sheep."

PORTE, L., CAPRON, A., SUREAU, P. & DERAN, C. A propos de la première observation clinique sérologiquement confirmée de fièvre Q à Madagascar. [**First Clinical Case of Q Fever Serologically Confirmed in Madagascar**] *Bull. Soc. Path. Exot.* 1959, Jan.–Feb., v. 52, No. 1, 78–82.

STOENNER, H. G., JELLISON, W. L., LACKMAN, D. B., BROCK, D. & CASEY, Mary. **Q Fever in Idaho.** *Amer. J. Hyg.* 1959, May, v. 69, No. 3, 202–13, 3 figs.

Human cases of Q fever were first recognized in Idaho in 1951; 131 sporadic cases (122 in males) have been diagnosed up to now. A survey revealed that the incidence of antibodies for *Rickettsia burneti* was highest among persons who were in occupational contact with sheep (15 positive sera out of 68). Of the 131 cases mentioned above, 36 patients (27%) had been in contact with sheep only and 24 (18%) in contact with cattle only. A significant percentage of patients were non-agricultural workers. Surveys of dairy cattle have shown a rise in the proportion of milk samples containing agglutinins for *R. burneti* from 1% in 1951 to 17% in 1958. "Although the organism was recovered from both cattle and sheep, epidemiologic studies indicated that sheep were the principal source of environmental contamination." *R. S. F. Hennessey*

KULAGIN, S. M., FUKI, A. D., ZUBKOVA, R. I. & POPOVA, L. D. **Two-Dose Vaccination against Q Fever.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 11, 1730–34. [Translated from Russian.]

A *Rickettsia burneti* vaccine which had been stored for 3–4 months caused reactions in 39·1% of persons who received an initial dose of 0·25 ml.; after storage for 15 months, the incidence of reactions to an initial dose of 0·5 ml. was 8·2%. The sera of 70–80% of persons inoculated with 0·5 ml. and 1·0 ml. (2-week interval) of the 15-month-old vaccine contained complement-fixing antibody up to 5 months after vaccination; at 8 months, the proportion of sera containing antibody was about 18%, compared with 47·3% for sera taken at 10 months from persons who had received 3 doses of 0·25, 0·5 and 1·0 ml. (weekly intervals) of the 3–4-month-old vaccine [this *Bulletin*, 1957, v. 54,

155]. "In order to simplify mass vaccination against Q fever, vaccination with 2 doses of 0·5 and 1 ml with a 2 week interval can be recommended."

R. S. F. Hennessey

BELIAKOV, V. D. & IL'CHENKO, A. A. **The Effectiveness of Combined Immunization against Intestinal Infections and Q Fever.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 11, 1734–9. [Translated from Russian.]

From epidemiological considerations, it has been concluded that the most effective means of controlling Q fever in Central Asia are measures to enhance specific immunity and that immunization should be carried out in the spring at the same time as inoculation against intestinal infections. Simultaneous immunization of guineapigs with Q fever vaccine and "polyvalent" and "tetravalent" vaccines [composition not stated, but apparently including antigens of *Salmonella* and *Shigella* spp. and tetanus toxoid] elicited antibody responses similar to those found after separate vaccination with the same preparations. There was evidence that the immunogenicity of tetanus toxoid was enhanced when the toxoid was given along with Q fever vaccine [the text and tabular data show some discord]. "Further study of the conditions of effective use of enteric vaccines and Q fever vaccine should be undertaken by epidemiological experiments."

R. S. F. Hennessey

YELLOW FEVER

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control.

DE RODANICHE, Enid, GALINDO, P. & JOHNSON, C. M. **Further Studies on the Experimental Transmission of Yellow Fever by** *Sabethes chloropterus.* *Amer. J. Trop. Med. & Hyg.* 1959, Mar., v. 8, No. 2, Pt. 1, 190–94.

In an extension of previous work [this *Bulletin,* 1957, v. 54, 674] on the experimental transmission of yellow fever virus by *Sabethes chloropterus* 2 virus strains were employed, the Trinidad 4202 strain and the C-10 strain (originally recovered from wild-caught *S. chloropterus* mosquitoes), and 2 hosts, rhesus monkeys and black spider monkeys. Successful monkey-to-mosquito, and subsequently mosquito-to-monkey, transfer of the virus was obtained only with the C-10 strain. It was also found that infection by mosquito bite did not take place after an extrinsic incubation period of 27 to 30 days, but did so after 34 to 37 days. A high titre of circulating virus was also necessary for infection of the mosquitoes to occur. It was concluded that *S. chloropterus* is a relatively inefficient vector.

E. R. Nye

COLLIER, W. A., DE ROEVER-BONNET, H. & HOEKSTRA, J. **A New Intracerebral Yellow Fever Mouse-Protection Test.** *Trop. & Geograph. Med.* Amsterdam. 1959, June, v. 11, No. 2, 167–73, 12 graphs. [17 refs.]

After briefly referring to the various methods developed since 1931 for performance of the mouse protection test in the detection of antibody to yellow

fever virus, the authors describe a new method in which such antibody can be demonstrated in immune serum by means of an intracerebral protection test. In application of this test the differences between the levels of the virulence curves of the controls and of the virus-serum mixtures are graphically reproduced. In the tests now detailed human immune sera and immune sera of white mice were investigated and in all but one of the test series the 17D vaccine strain of virus was employed.

For the performance of the test the contents of one or two ampoules of 17D vaccine were suspended in 1% bovine albumin in a 1 in 9 dilution. From these, dilution series of 1 in 90, 1 in 900, 1 in 9,000 and 1 in 90,000 were prepared; 0·9 ml. of each dilution was placed in a Wassermann tube and 0·1 ml. of serum was added to each tube, undiluted and in dilutions of 1 in 10 and 1 in 100; 0·1 ml. of 1% bovine albumin was added to the control tubes. In each test the final dilutions were, therefore, 1 in 10, 1 in 100, 1 in 1,000, 1 in 10,000 and 1 in 100,000 for virus and 1 in 10, 1 in 100 and 1 in 1,000 for serum. The tubes were shaken, kept at room (±20°C.) temperature for 30 minutes and then placed in an ice-water bath. 0·02 ml. of each dilution was injected intracerebrally into 5 or 6 mice, which remained under observation for 3 weeks, until the test was terminated. The LD50, by the method of Reed and Muench, was calculated every day from the number of dead mice, and the figures thus obtained were plotted on a virulence curve.

Results of the tests showed conclusively the influence of the antibodies present, even in weakly immune sera, on the course of virulence. As indicated in the graphs, the greater the distance between the virulence curves of the controls and those of the virus-serum mixtures, the stronger the immunity present in the serum. In the authors' view, reproduction of the degree of immunity by elaboration of the virulence curves is decidedly clearer than the usual calculation of the LD50 at the end of the test and the immunity index calculated from it. In the latter case the result is a single figure, whereas by means of the virulence curves different factors may be compared: (a) the slower course of the entire illness (incubation period *plus* duration of manifest illness); (b) the change of the rate at which the disease takes its course, or the rate at which the curve rises; and (c) the absolute level of the virulence at the end of the test. Finally, as a result of their comparing the influence of a weakly immune human serum on the 17D vaccine strain, the 17D neurotropic strain, the Asibi strain and the neurotropic Dakar strain, the authors recommend the use of one or other of the 2 first-named for carrying out the test.

G. Stuart

DENGUE AND ALLIED FEVERS

Hotta, S. **Propagation of Dengue Virus in Tissue Culture.** *Acta Tropica.* Basle. 1959, v. 16, No. 2, 108–50, 17 figs. [Numerous refs.]

Rhesus testicular and kidney tissue in plasma clot cultures and in trypsinized cultures was used. Dengue virus was shown to disappear within 24 hours in tubes without cells incubated at 35°C.

In rhesus testicular tissue, the virus persisted for as long as 77 days, but

did not appear to multiply significantly and could not be passaged successfully. No significant morphological changes were seen in the cultures.

In rhesus kidney plasma clot cultures the virus persisted for at least 32 days and there was suggestive evidence of multiplication of the virus.

In trypsinized kidney cells the virus multiplied, reaching a maximum titre of about $10^{-4.7}$ on the 10th day of incubation. 40 passages of dengue-1 virus with titres of about 10^{-5} were achieved. Results were less regular with dengue-2 virus. Degenerative changes began to appear in the kidney tissue cultures 5 to 7 days after inoculation. Some of the cells became spherical and of increased density. By 10 days the cell population was reduced to about half and at 2 weeks only a sparse population of cells remained. Some of these cells had long slender strands or contained dense cytoplasmic masses. Even after 2 weeks, however, there were normal-looking cells visible.

Virus titration in tissue cultures with dengue-1 virus gave titres very close to those obtained in mice. Deaths were irregular with the dengue-2 virus and the results are difficult to interpret. It was found possible to carry out neutralization tests with dengue-1 virus.

Trypsinized human kidney cells were used in a single experiment. There was no definite evidence of multiplication of the virus, although it persisted for at least 15 days. No morphological changes were observed. During this work, a cytopathogenic agent from rhesus kidney causing foamy cell-changes was isolated. [This paper might with advantage have been shortened.]

C. E. Gordon Smith

RABIES

DAVIES, A. M. **[Rabies in Israel]** *Harefuah*. Jerusalem. 1959, July 1, v. 57, No. 1 [In Hebrew 8–9, 1 chart. (27 refs.) English summary 9–10].

The English summary appended to the paper is as follows:—

"1. Between the years 1948–1957, 23 cases of human rabies have been notified to the Ministry of Health. 14 were caused by the bites of dogs, 5 by jackals, one by a fox and one by a cat. In two cases, the origin of the infection is not known.

"2. During the same period, 50,000 persons who had been bitten or were in contact with suspected rabid animals, applied to District Health Offices for advice. 17,000 were sent for a course of vaccine injections.

"3. 1,153 animals examined were positive for rabies; 63% of them dogs, 17% bovines and 9% jackals.

"4. A summary is given of the principles of treatment and of recent advances in this field. During the years 1953–56, there were 16 cases of reaction to Semple type vaccine, 11 of them neuropathies. This gives a complication rate of 2·1/1000 treatments.

"5. It is estimated that the wild dog population of Israel is 100,000–150,000. The present dog eradication programme succeeds merely to prevent the natural increase, leaving the basic population untouched.

"6. The low incidence of rabies is a result of the very high cost of treatment which is calculated to have amounted to over a million pounds during the first 10 years. A much smaller sum, spent on prevention, would probably have achieved more."

SUREAU, P., LEMAITRE, Y. & RAKOTOMANGA, J. C. Premier cas de rage observé à Madagascar chez un chien préventivement vacciné avec le vaccin avianise "souche Flury". [**First Case of Rabies seen in Madagascar in a Dog Vaccinated with Flury Strain Avianized Vaccine**] *Bull. Soc. Path. Exot.* 1959, Jan.–Feb., v. 52, No. 1, 15–19.

See this *Bulletin*, 1957, v. 54, 1184.

GOLDWASSER, R. A., KISSLING, R. E., CARSKI, T. R. & HOSTY, T. S. **Fluorescent Antibody Staining of Rabies Virus Antigens in the Salivary Glands of Rabid Animals.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 4, 579–88, 4 coloured figs. on pl.

In a previous article GOLDWASSER and KISSLING [this *Bulletin*, 1958, v. 55, 1319] described techniques for the staining with fluorescent antibody of street and fixed rabies antigens in the brains of experimentally infected mice and indicated that the same techniques could be employed to detect the presence of rabies antigens in the salivary glands of infected animals. The present article gives details of further investigations into the staining of virus antigens in the salivary glands of rabid animals and presents the results of a study of material submitted for rabies diagnosis in the State of Alabama over a 5-month period in 1958—a study in which the salivary glands of various animal species were processed with fluorescent antibody, their brains examined for the presence of Negri bodies and their brains and salivary glands subjected to the biological (mouse inoculation) test for isolation of the virus.

In the first part of the study, in which 121 animals (100 dogs) were investigated by these methods, only 2 smears from the salivary glands of each animal were made on slides for staining with fluorescent antibody. Of the 121 animals investigated 94 proved to be non-rabid on histological examination and on biological testing; negative findings by fluorescent staining were also obtained in all 94. By virus isolation from the brain the remaining 27 were proved to be rabid and of these, 24 showed Negri bodies in the brain, while 25 were found to excrete virus in the salivary gland. Fluorescent antibody staining was, however, found in only 19 (76%) of the 25 glands from which virus was isolated. An explanation of these negative findings was, therefore, sought and as in this connexion it had been noted that in several cases one of the 2 slides made from the same gland was found to contain fluorescein-stained antigen, whereas the other showed very little or no antigen, the possibility was considered that an unequal distribution of the virus in the glands might afford the desired explanation.

In order to test this possibility, therefore, another series of preparations were made and obtained, but this time 6 slides were prepared from each of the sets of glands selected, the authors using a separate piece of tissue cut from a different area of the gland for each slide. Results of this, the second part of the study, (a) afforded convincing proof that the virus was not distributed

uniformly throughout the salivary gland tissue and that it might be present in considerable concentration in one area and absent from another (as evidenced by the fact that in several instances a slide made from one area showed little or no staining, whereas another slide made from another area showed considerable antigen to be present) and (b) showed that in the case of 49 animals, from the salivary glands of which virus was isolated by animal inoculation, 48 revealed antigens in the glands stained by fluorescent antibody techniques, while the one in which diagnosis by this method was missed contained only traces of virus.

In discussing the conclusions to be drawn from the results of their present study, the authors stress the speed and specificity of fluorescent antibody techniques for determining the presence of rabies virus in the salivary glands of biting animals. Diagnosis by this method enables a decision regarding vaccination of the bitten person to be reached within 24 hours of the arrival of suspected material in the laboratory and provides obvious advantages over the diagnostic methods ordinarily in use: virus isolation, which is time-consuming [requiring 8–12 days], and histological examination of the brain, which fails to reveal the presence of Negri bodies in a considerable number [10–15%] of known positive brain specimens. "Considerably wider application of this method is needed", however, "before it would be possible to determine whether the standard methods for the diagnosis of rabies in use today . . . could be replaced by fluorescent antibody techniques."

G. Stuart

VONDRÁCKOVÁ, A., VÝMOLA, F., VORTEL, V., ONDRÁCEK, J. & KRÁL, L. Atypická forma lyssy. [**Atypical Form of Hydrophobia**] *Časopis Lékařů Českých*. Prague. 1959, July 17, v. 98, Nos. 29/30, 933–7, 3 figs. [21 refs.]

The English summary appended to the paper is as follows:—

"The authors present a report of a paretic form of hydrophobia, diagnosed post-mortem by a virologist and pathologist and attempt to detect criteria which could lead to a correct diagnosis intravitam. Neuroplegy did not prevent the progress of the disease and its fatal outcome. An account is given of the results of the virological examination and the pathological findings."

JELESIC, Z. & JOVANOVIC, Ljubica. [**Protective Value of Antirabic Vaccination and Problems of its Practical Application. Shortening of the Rabic Incubation after Parenteral Application of Serum in Experimental Animals**] *Med. Pregled*. Novi Sad. 1958, v. 11, No. 3, 151–5. [In Serbian.]

The English summary appended to the paper is as follows:—

"The authors experimentally prove that the formerly described shortening of rabic incubation in mice, which were infected with i. m. applied virus and treated with i. p. applied serum is to be explained by nonspecific sensibilisation by means of parenteral foreign proteins. Even the gamma-globulins of the normal as well as of the antirabic serum exhibit the similar effect, but larger quantities of rabic antibodies may prevent the appearance of this sensibilisation.

"On the grounds of their own observations the authors are of the opinion

that the treatment of men with nonpurified or insufficient quantities of purified antirabic serum may be followed by shortening of rabic incubation (*i.e.* opposite effect of the supposed one). To the same conclusion point also some cases of human rabies after combined treatment with antiserum and vaccine.

"Two problems are to be solved before definite introduction of serum prophylaxis besides classical vaccine prophylaxis of human rabies: optimal quantities of purified gamma-globulins in the antirabic serum and the establishing of a treatment which would eliminate or minimize the interference between the passive applied antibodies and antigens (vaccines)."

PLAGUE

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, rodent hosts, transmission, pathology, diagnosis, clinical findings, treatment, control.

MACCHIAVELLO, A. Estudios sobre peste selvática en América del Sur. V. Peste selvática en Bolivia. Consideraciones generales sobre la geografía e historia de la peste. [**Studies on Sylvatic Plague in South America. V. Sylvatic Plague in Bolivia**] *Bol. Oficina Sanitaria Panamericana.* 1959, June, v. 46, No. 6, 509–24. [74 refs.] English summary.

[For references to earlier papers, see this *Bulletin*, 1959, v. 56, 155.]

"The inland location of Bolivia explains why that country was the last in South America to be invaded by plague. The first three foci (apparently of independent origin) were sylvatic: the first occurred in Tarija in 1921; the second—although recognized officially as being the first—was found in Vallegrande in 1928; and the third and last, in Tomina in 1933.

"The invasion into the low eastern area of the Chaco, along the spurs of the Andes Mountains, occurred later; first as a result of the oil explorations and, later, the Chaco War, both of which favored the penetration, development, and spread of murines of the genus *Rattus*. Beginning in 1938 murine plague became entrenched in the area and caused violent epidemics, preceded by epizootics.

"Several explanations have been given for the establishment of plague in the three above-mentioned areas. The most reliable was that the infection came from Argentina, since in 1920 the disease caused serious epidemics in Jujuy Province, from which the infection spread to Tarija. It is possible that supplies for the oil camps favored the spread of the infection to Vallegrande; the construction work on the Camiri-Sucre road might have been responsible for the spread to Tomina.

"Plague in the southern area has become somewhat altered as a result of the *Rattus* invasion; its originally sylvatic characteristics are now considered secondary and they are seldom mentioned. The other two sylvatic foci continue active, but without the dramatic effects of the early years. This is due in large measures to the activities of the Antiplague Service, which uses DDT extensively, and to the house-spraying carried out constantly by the Antimalaria Service. Fleas are destroyed through these activities, although the

enzootic continues in the wild areas and human cases occur occasionally in houses located in the most remote districts.

"Contrary to what occurs in other sylvatic plague areas, the first observers of the three aforesaid foci denied the fact that wild rodents might have been responsible for them; rather they favored the theory of extensive and intensive inter-human transmission of the infection. According to the Bolivian investigators, these foci of plague, ecologically sylvatic, did not then conform to a sylvatic epidemiology but rather to plague developed exclusively at the inter-human level, transmitted probably by *Pulex irritans*, although this was never confirmed. Later, the idea was accepted that the infection had passed from man to the wild rodent, that is, that the infection had become secondarily sylvatic in the epidemiological sense.

"The article presents the problem with the purpose of clarifying it in subsequent papers based on field investigations and on the study of extensive literature, for the most part unpublished. In addition, preliminary data are given on plague epidemics and on the distribution of known rodents and fleas up to 1952, as well as a list of references, perhaps the most complete compiled to date."

GIRARD, G. Sur la production de concrétions cristallomorphes de nature protidique par une souche de *Pasteurella pestis*. [**Production of Crystalline Concretions of a Protein Nature by a Strain of** *Pasteurella pestis*] *C.R. Soc. Biol.* 1959, v. 153, No. 2, 277–9.

MANIGAULT, P. Observation au microscope des productions cristallines de la souche *Pasteurella pestis* EV (Girard et Robic). [**Microscopic Observations on the Crystalline Concretions produced by** *Pasteurella pestis*, **Strain EV**] *Ibid.*, 279–80, 1 fig.

These two short notes deal with the curious whitish crystalline concretions that develop in certain agar cultures of a particular strain of the plague bacillus. This bacteriological curiosity, which is peculiar to the EV strain of *Pasteurella pestis* cultured under certain conditions, has been known for some time and the development of these bundles of long crystals in the medium on which the organism is cultivated has no obvious explanation and the significance of the concretions is unknown. The figure in the second paper is a photomicrograph of a group or bundle of the crystals.

It will be recalled that *P. pestis* EV, sometimes known as the Girard-Robic strain, became attenuated after monthly subculture for some years and has been used as a living vaccine for plague prophylaxis; it was used in the Madagascar trials reported by ROBIC in 1938 [this *Bulletin*, 1939, v. 36, 314].

H. J. Bensted

DODIN, A. & BRYGOO, E. R. Activité succinodeshydrogenasique de *Pasteurella pestis*, souche E. V. I. Étude colorimetrique. [**Succinodehydrogenase Activity of** *P. pestis*, **Strain EV. I. Colorimetric Study**] *Arch. Inst. Pasteur de Madagascar.* 1959, v. 27, 13–16, 2 graphs.

See also p. 1134, KOROBKOVA *et al.*, **A Study of a Combined (Mixed) Vaccine from Dead** *Vibrio comma* **and Live** *Pasteurella pestis*.

GIRARD, G., with the technical collaboration of A. CHEVALIER. Réaction de la souris blanche splénectomisée à la peste expérimentale et à l'immunisation par le virus-vaccin EV. [**Reaction of Splenectomized White Mice to Experimental Plague and to Immunization with EV Vaccine**] *Bull. Soc. Path. Exot.* 1959, Jan.–Feb., v. 52, No. 1, 13–15.

Splenectomy of white mice does not modify the picture produced by inoculating these animals with a virulent strain of *Pasteurella pestis*. The acute infection with septicaemia, necrotic masses in the liver and other characteristic post-mortem appearances were not different from those seen in the control animals. When, however, active protection tests of the EV vaccine in splenectomized and non-splenectomized mice were compared it was found that in the first place approximately 25% of the splenectomized mice became infected after inoculation with this living attenuated vaccine, compared with 5% of the non-splenectomized animals. In the second place the protective effect of the EV vaccine was significantly greater in the latter group of animals; the non-splenectomized were about 5 times better protected against a virulent challenge by the EV vaccine than the splenectomized mice. *H. J. Bensted*

CHOLERA

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

BHATTACHARJI, L. M. & MAJUMDER, N. **Some Observations on the Epidemiology of Cholera in Calcutta during 1958.** *Alumni Ass. Bull.* Calcutta. 1959, Apr., v. 8, No. 12, 18–31, 6 charts.

Cholera appears only to affect those living in close proximity to an active case of the disease, and pathogenic vibrios can only rarely be isolated from natural waters in an endemic area. In the case of the Hooghly river, KRISHNAN was able to isolate *Vibrio cholerae* from only 1·07% of 837 samples of its water obtained between 1951 and 1953. The maximum period of survival of cholera vibrios in such river water has been shown in a Bengal study not to exceed 16 days.

In Western Bengal an endemic area is formed by the deltas of the Hooghly, Damodar and Rupnarain rivers, and in the midst of this insalubrious area Calcutta and its smaller twin city, Howrah, are situated. This paper examines the epidemiology of cholera in the city of Calcutta during 1958, and refers to earlier records of the disease in the same area.

The gross annual deaths from cholera fell abruptly after the introduction of a piped, filtered water-supply in 1870, but, nevertheless, annual epidemics of varying severity have continued to occur between the third week of March and the end of August, the peak period being at the end of April. After a 4-year period of declining incidence, a relatively severe epidemic occurred in 1958 with 4,866 notified cases (up to November) and 1,747 deaths, the attack rate being 1·72 and the death rate 0·61 per mille of the population.

Both sexes and all age-groups were affected, a little over half the patients

being over 16 years of age, while infants and children below the age of 5 years constituted 28·1% of the victims. [No indication of the structure of the population by age-groups is given, however.] The mortality was highest in infants and young children, but the overall case mortality approached 40%.

The epidemic began diffusely throughout the whole city, but eventually it was seen that the greater number of cases arose in those wards which were situated on the banks of the Hooghly or were traversed by canals. Overcrowding did not appear to be an important epidemiological factor, but inadequate housing did, in that the highest incidence of the disease fell upon those areas in which the greatest proportion of people lived in " bustees " [bustee = a small village, and a " bustee-dweller " must presumably be one who lives in a hut, not in a permanent house]. The disease appeared to attack equally those who obtained their water from a tap or tube-well and those who drank from canals, but those who drank crude water from street hydrants [evidently provided for street-washing and fire-fighting purposes] appeared to run a peculiar risk, the attack rate in this small series being 50%. The type of latrine available did not influence the attack rate [though both water closets and hand-emptied privies were grossly over-patronized] but a significantly higher attack rate occurred in households which had no latrine at all. There was a higher incidence of cholera in those who purchased their mid-day meal outside than among those who ate it at home. The importance of poor environmental sanitation was clearly demonstrated by the fact that 48% of those affected spent their time at home, while office workers contributed 36%, labourers and artisans 4% and students 2% of the patients. Hindus were proportionately more frequently affected than other communities and this was attributable to their predilection for frequent bathing in infected waters. Out of 504 cholera patients under special investigation, only 14·28% had received anti-cholera vaccine previously, and in these vaccination had been performed either 6 months or less than one week before the onset of their disease.

[This sombre paper depicts the epidemiology of cholera in all its squalid detail.] *J. H. Walters*

FERREIRA, M. O Doutor António da Costa Carvalho e a epidemia do cólera em Timor [1893]. [**Da Costa Carvalho and the Epidemic of Cholera in Timor, 1893**] *Anais Inst. Med. Trop.* Lisbon. 1957, Sept.–Dec., v. 14, Nos. 3/4, 547–75, 1 fig. on pl.

MUKERJEE, S. **Identification of S-R Dissociation of the Strains of** *Vibrio cholerae* **by Group II Bacteriophages.** *Ann. Biochem. & Exper. Med.* 1959, Jan., v. 19, No. 1, 9–12, 2 figs.

Rough [R] cultures of cholera vibrios are usually identified by their cultural characters, stability in saline and agglutinability in Millon's reagent or in flavine solutions. More specific tests depend on serological reactions with highly absorbed pure Inaba and Ogawa O sera used in conjunction with a R serum which has been heavily absorbed with living suspensions of Inaba and Ogawa vibrios. These procedures will make possible the detection of incomplete S–R dissociation.

Recently it has been found that Group II cholera bacteriophages are lytic only for the smooth elements of vibrio cultures and it is therefore possible to study S–R dissociation quantitatively by measuring the optical density of cholera cultures after exposure to the action of the Group II phages. This method will not only differentiate between R and S cultures but in comparative tests of mixtures of R and S organisms the differences in lysability will be in accordance with the proportion of the two types in the mixture.

H. J. Bensted

LIU, P. V. **Studies on the Hemolysin of** *Vibrio cholerae*. *J. Infect. Dis.* 1959, May–June, v. 104, No. 3, 238–52, 11 figs. [15 refs.]

In spite of the various conflicting reports regarding the production of haemolysin by cholera vibrios, the general consensus of opinion is that this organism does not produce a soluble haemolysin which would liberate haemoglobin from a suspension of red blood cells in the absence of the vibrios themselves. The El Tor vibrio, on the other hand, does produce a heat-labile soluble haemolysin which is antigenic—immunized rabbits yield sera containing neutralizing antibody against it [this *Bulletin*, 1942, v. 39, 838].

The author has shown, however, that cholera vibrios can produce, under certain conditions, and in very low titre, some extracellular haemolytic substance, the chemical nature of which has not yet been determined. This substance injected into animals produces a tissue reaction identical to that seen after the injection of a suspension of heat-killed vibrios, whereas the haemolysin of El Tor vibrios produces a characteristic haemorrhagic lesion.

The reported haemolysis seen in blood-agar plate cultures of *Vibrio cholerae*, he found to be due to the high *p*H around the colonies (produced by the growth of the organisms) which led to destruction of the red blood cells and denaturation of the released haemoglobin—the "haemodigestion" of other workers [*ibid.*, 1913, v. 1, 450]. Similarly, he investigated the reported haemolysis when peptone-water cultures of *V. cholerae* were used for the test with suspensions of red blood cells in normal saline. This he found was due to the hypotonicity of the mixture; the final concentration of NaCl was less than 0·45%. The observed haemolysis was therefore due to the sensitivity of the older red cells to this low salt concentration and not to haemolysin from the culture.

[This is a valuable paper and confirms one's own opinion, and that of many others with similar experience, that the haemolytic test devised by GREIG [*ibid.*, 1914, v. 3, 477; 1915, v. 6, 36] did truly differentiate between the El Tor vibrio and *Vibrio cholerae*.]

H. J. Bensted

TAKAISHI, K. [**Morphological and Immunochemical Studies on the Cell Wall of** *Vibrio cholerae*] *Shikoku Acta Med.* 1959, Mar., v. 14, No. 3, 354–81, 8 pls. & 2 figs. [81 refs.] [In Japanese.] English summary.

The author, from Tokushima University School of Medicine, Japan, studied the cell wall and cytoplasm of *Vibrio cholerae*, with the following results, which are recorded briefly in a summary in English. Bacteriolysin was produced by cell wall antigen but not by cytoplasm antigen. Lysis of the cell

wall occurred when both the isolated cell wall and the whole cell were used, so that the author considers that bacteriolysis is in fact " lysis of bacterial cell wall ".

Group-specific and type-specific antigens were found in the cell walls of Inaba, Kamata and Hikojima strains and in that of water vibrio 2.

Cell walls of all 4 strains contained about 10·3–11·3% N and 0·9–1·0% P. Total lipids were 14·4–16·3% in the *Vibrio cholerae* strains, but only 0·25% in the water vibrio. On the other hand the cell wall of the water vibrio contained the largest amount of carbohydrate (34·4%) and that of the Inaba strain the smallest (14·3%).

The amino-acid constituents of the *V. cholerae* cell wall resembled those of other Gram-negative bacteria and there were no significant strain differences: but there were significant variations in the monosaccharide constituents of the cell walls. Glucose was common in all four strains, but lactose, galactose, xylose and rhamnose were not.

Injection of *V. cholerae* cell wall or cytoplasm produced protective antibodies in mice, and the protective power was about the same with both kinds of antibody. However the cytoplasm vaccine was more toxic than that of the cell wall and it is concluded that a cell wall vaccine prepared from *V. cholerae* is very efficient. *H. J. O'D. Burke-Gaffney*

MUKHERJI, A. **Toxin Production and Virulence of Inaba and Ogawa Vibrios.** *J. Immunology.* 1959, May, v. 82, No. 5, 381–4. [12 refs.]

During the preparation of anti-cholera sera, by the injection of rabbits intravenously with living cultures of Inaba and Ogawa strains of *Vibrio cholerae,* it was noted that the mortality among the rabbits receiving injections of the Inaba strain was about 15% whereas with those injected with the Ogawa vibrios the mortality was 65%. The toxic manifestations in the rabbit, such as the shedding of the intestinal mucous membrane etc., were much more marked in the case of the Ogawa strain. Mouse virulence tests confirmed that the Ogawa strains were more virulent.

It was found that the addition of tryptophan to the media increased the toxicity of the cultures.

After about 16 hours' incubation the toxicity was about maximal, and as incubation was prolonged cultures were found to be less toxic. Maximum toxicity could be preserved for long periods by storing cultures at –10°C.

[It is not very obvious from the account given how long the various strains used had been cultivated on artificial media; virulence tends to fall off fairly rapidly in laboratory cultures. Virulence and toxicity do not necessarily go hand in hand; but as all the tests reported here appear to have been done on whole cultures it is difficult to assess the results.] *H. J. Bensted*

BANERJEE, S. & BHADURI, J. N. **Serum Protein-Bound Carbohydrates and Lipids in Cholera.** *Proc. Soc. Exper. Biol. & Med.* 1959, June, v. 101, No. 2, 340–41. [16 refs.]

" Serum glycoproteins, mucoproteins, phospholipid, total lipid, total cholesterol and lipoproteins were determined in patients suffering from cholera

and in normal subjects. In cholera serum glycoproteins, mucoproteins, phospholipids, total lipids and β-lipoproteins were significantly increased and α-lipoproteins and total cholesterol were diminished."

NIKONOV, A. G. **Concerning the Pathogenesis and Diagnosis of the Persistent Carrier State in Persons recovering from Cholera.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, Nos. 1/2, 40–44, 1 fig. [Translated from Russian.]

Although the carrier state in cholera is comparatively rare, the author attaches considerable importance to it as epidemics have been caused by persons who have had cholera 6 to 8 months previously. It is possible that such a carrier state plays an important part in preserving the causative agent of the disease between epidemics in places where cholera is endemic.

Experiments were conducted by injecting small doses of the *Vibrio cholerae* directly into the gall bladder of rabbits where it was found the organisms multiplied rapidly though the animals showed no visible signs of disease. The vibrio was found in the bile, liver and small intestine of animals killed at different periods after infection, but not in the blood or in other internal organs. Though the organism was found in the small intestine of animals killed it was not discovered in the faeces of the animals while alive. During the first 2 weeks it was constantly found in the bile, but later began to disappear though in some animals it persisted for as long as 7 months.

An immune serum administered before injection of the organism did not protect the animal against infection, consequently its destruction in rabbits which acquired immunity as a result of prolonged existence of the vibrio in the biliary system could not be due merely to bactericidal properties of the blood. It must be due to some additional factors absent in passively immunized animals.

Similar experiments on guineapigs seemed to indicate that growth in the biliary system of animals leads to transformation of the organism into " rough " forms which are not adapted to parasitic existence in the animal and are therefore destroyed. This distinguishes the cholera vibrio from *Salmonella typhi* which does not exhibit this kind of variation in the animal body.

It is quite likely that a protracted carrier state among persons recovering from cholera is more frequent than is generally believed. The most reliable method of diagnosing the carrier state is examination of the bile (duodenal contents) as in typhoid and moreover attention must be paid to R type colonies which are markedly different from typical colonies of *V. cholerae* and are easily mistaken for colonies of adventitious organisms. R type organisms are able to dissociate rapidly on entering an animal body and give rise to virulent S type organisms. *P. A. Clearkin*

MUKHERJEE, A. M. & NEOGY, K. N. **Observation of Morbid Changes in Mice after Experimental Inoculation with** *Vibrio cholerae*. *Calcutta Med. J.* 1959, Apr., v. 56, No. 4, 120–22, 6 figs. on 2 pls.

The intraperitoneal injection into mice of 250×10^6 cholera vibrios (living cultures of epidemic strains isolated the previous year) resulted in the death

of 80% of the animals in 12–18 hours. There was little evidence of cellular reactions in the organs but they all showed various degrees of congestion. There was generally a simple fluid exudate in the pleural cavity and the lungs were oedematous, and although there was some cellular reaction in the alveolar walls it does not appear to have been intense. The small gut was slightly congested but the large intestine showed no abnormalities. *Vibrio cholerae* was readily isolated from the speen, liver and heart blood. *H. J. Bensted*

KOROBKOVA, E. I., VERENINOVA, N. K., KALACHEVA, N. F., PETROVA, B. I. & KRAINOVA, A. N. **A Study of a Combined (Mixed) Vaccine from Dead** *Vibrio comma* **and Live** *Pasteurella pestis*. *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 11, 1745–51, 3 figs. [Translated from Russian.]

Killed cholera and living plague vaccine dried in saccharose-gelatin was found to be highly immunogenic and to retain its potency over long periods. Guineapigs immunized with this mixed vaccine were found to be well protected when subsequently challenged with virulent strains of *Pasteurella pestis* and *Vibrio cholerae*. The combined vaccine appeared to protect guineapigs more efficiently against cholera than the monovalent killed cholera vaccine. The agglutinin response in rabbits immunized with the combined and the separate monovalent vaccines was of the same order. *H. J. Bensted*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

SHARMA, R. **Effect of Cholesterol on the Growth and Virulence of** *Entamoeba histolytica*. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1959, May, v. 53, No. 3, 278–81. [10 refs.]

Previous workers have suggested that cholesterol is a growth factor for *Entamoeba histolytica* [this *Bulletin*, 1944, v. 41, 216; and 1949, v. 46, 40]. The effects of this substance on growth and invasive power of *E. histolytica* have now been studied. The strain EA used was not capable of invading rat tissues after intra-caecal inoculation [*ibid.*, 1955, v. 52, 1087]. It was maintained in a standard diphasic medium with addition of rice starch, rice starch and cholesterol and cholesterol alone respectively. Note was made of the growth in these media and after 4 and 6 weeks material was collected from each and 0·3 ml. of pooled material used to infect rats intracaecally which were being fed a standard diet. After 1 week the rats were killed and the amount of tissue invasion noted. A group of 18 rats fed on cholesterol in olive oil (0·5 gm./kgm. per day) for 1 week were treated in the same way. Further groups of 6 rats were inoculated with pooled cultures of amoebae grown in presence and absence of cholesterol for different periods and the state of caecal wall and contents examined after 1 week.

The results showed that the strain of *E. histolytica* used failed to invade rat tissues when the rats were fed on a stock diet but was invasive and produced ulcers when cholesterol was present in growth medium or the animals received this substance in diet. The author concludes that cholesterol affects the virulence of this strain of amoebae, both rapidly and persistently. The rationale of this action, which may be direct or indirect, is not understood. The effect of cholesteral in diet as a factor in reactivating strains of *E. histolytica* is mentioned. *J. D. Fulton*

FLORES-BARROETA, F., NUÑEZ, V. & BIAGI F., F. Observaciones sobre amibiasis en material de autopsia. Estudio de 109 casos. [**A Study of 109 Cases of Amoebiasis Observed at Autopsy**] Reprinted from *Prensa Med. Mexicana.* 1959, Mar.–Apr., v. 24, Nos. 3/4, 6 pp., 1 chart. [12 refs.]

The authors, in Mexico City, observed 109 cases of amoebiasis in 2,202 autopsies carried out between 1954 and 1958. They discuss their findings and set out the results in 13 tables. In the first 2½ years the lesions were studied by ordinary histological methods: thereafter, more specifically parasitological examinations were made, namely direct and concentration studies of stools, and direct and culture examinations of ulcers and of normal liver in the intestinal forms, and of the abscess cavity and pus in the cases of liver abscesses.

The classification of autopsy material is tabulated according to aetiology on criteria described. The lesions were divided in this way into (1) amoebic (2) undetermined aetiology and (3) others, in both ulceration of the colon and in liver abscess: in the former case an additional category of "probably amoebic" was included. An amoebic origin was determined in 72 (3·3% of all autopsies) cases of ulceration of the colon and in 92 (4·2% of all autopsies) of the liver abscesses.

Exclusively intestinal amoebiasis showed little variation with age, but liver abscess was much commoner between the ages of 31 and 50. Similarly the intestinal form showed an equal sex distribution, but liver lesions were commoner in men. There were only 2 carriers of amoebae without lesions.

12·8% of lesions were solely intestinal, 31·2% were solely hepatic and 53·2% were found in both sites. Of the intestinal lesions, 77·8% were in the caecum. 84% of liver lesions were in the right lobe.

The number of abscesses in the liver varied from 1 (46·7% of cases) to more than 36 (1·1%). Two or more abscesses were seen in more than one-half the cases. The diameter of the abscesses varied from 0·1 to 30 cm.: 84·4% were less than 17 cm. in diameter. Complications were seen in 60·8% of the 92 liver abscesses: the commonest were rupture into the peritoneum (30·4%), pleura (22·8%) and lung (15·6%). Amoebae were found in 71 of the 92 abscesses: only 16 of the patients concerned had received specific treatment, compared with 15 of the 21 patients in whose abscesses amoebae were not found.

H. J. O'D. Burke-Gaffney

FOLL, C. V. & GAME, B. P. **Treatment of Amoebiasis in Upper Burma.** *J. Trop. Med. & Hyg.* 1959, July, v. 62, No. 7, 173–6.

The incidence of *Entamoeba histolytica* infection in the people of Upper Burma is very high; 46% of women attending antenatal clinics have been

found to be infected. 10 days' emetine-bismuth-iodide [EBI] treatment in hospital is curative, but it is impracticable. One of the authors has already reported [this *Bulletin*, 1958, v. 55, 162] on a trial of Entamide as a feasible alternative; this paper extends the report on this drug, and also on Entamide benzoate, Entamide piperazine sulphate, two other Entamide combinations, EBI, and Nivembin. The total number of patients treated was 288, 130 of them being outpatients. Single stools were examined at monthly intervals for 3 months after the various treatments; the relevant data are set out in a table. 3 months after treatment with one or other of the Entamide preparations 40% to 70% were found to harbour parasites (relapses or re-infections); after EBI alone, or Entamide followed by Nivembin, the infection rate was only one-third of those treated. The numbers in each group treated ranged from 5 to a maximum of 61, and those followed up 5 to 55. [These and the scanty and infrequent stool examinations, the authors appreciate, may give a misleadingly optimistic picture of the immediate effectiveness of the treatments, while re-infection may reverse it.]

The authors think that all cases of symptomless amoebiasis should be treated [but they offer no practical solution of a problem of such magnitude].

A. R. D. Adams

Donckaster, R., Donoso, F., Martinez, Perla & Thumala, A. Ensayo terapéutico de la amibiasis intestinal crónica con Pontalin (Win 5047). [**The Effect of Pontalin (Win 5047) in Chronic Intestinal Amoebiasis**] *Bol. Chileno de Parasit.* 1959, Jan.–Mar., v. 14, No. 1, 2–4. [16 refs.]

The English summary appended to the paper is as follows:—

"1.—The therapeutic action of Pontalin on 80 cases of chronic amebiasis is reported. Children received 0·05 to 0·10 gm. per kilo and adults 0·75 to 4·00 gm. daily. With the exception of one group treated during 8 days, all patients were administered the drug for 10 days.

"2.—Three parasitological controls were performed every other day 10–30 and 90 days after treatment with the combined Telemann's and P.V.A., fixation procedures.

"3.—49·5 and 51·1% of the patients were negative for *E. histolytica* at the 10th and 90th day controls. No differences on these results were observed with the various therapeutic schemes used.

"4.—All patients, including children, tolerated the drug well.

"5.—Emphasis is laid upon the good controls provided by the methods used and the conclusion is reached that the use of Pontalin in the treatment of chronic amebiasis is not justified."

[See this *Bulletin*, 1957, v. 54, 822.]

Lynch, J. E., Margison, Joan E. & Nelson, Barbara V. **The Effect of Tetracycline-Oleandomycin (Signemycin) against Experimental Amebiasis in Rats.** *Antibiotics & Chemotherapy.* New York. 1959, May, v. 9, No. 5, 294–300, 2 figs.

It has usually been found that antibiotics with antibacterial properties affect *Entamoeba histolytica* in culture through this property [this *Bulletin*, 1954, v. 51, 928; 1955, v. 52, 977; 1956, v. 53, 1342, 1343]. Tetracycline and oleandomycin have not proved exceptional in this respect. The present investigation

was carried out with these substances in combination in weanling rats. The activity of each component was first measured alone as a preliminary. 846 female rats weighing 35 to 40 gm. were used along with strain 200F of *E. histolytica* which is accompanied by a mixed bacterial flora. Intracaecal inoculations of 0·3 ml. culture material containing approximately 10^5 parasites were used. Drug treatment was started 24 hours after inoculation and continued daily for 5 days at different levels. At autopsy 48 hours later, the state of infection was determined by macro- and micro-examination. The results are summarized in tables. A mixture of 67% tetracycline and 33% oleandomycin exhibited markedly higher activity at every level studied than each antibiotic alone.

J. D. Fulton

YAWS AND OTHER TREPONEMATOSES

HACKETT, C. J. **Epidemiology of Receding Yaws.** *J. Trop. Med. & Hyg.* 1959, July, v. 62, No. 7, 153–7, 1 chart.

Yaws has declined, both in incidence and severity, not only in areas where mass campaigns have been conducted but also those in which only improvement of general hygiene and economic state has occurred, in particular, by the areas becoming less remote. The reduction in severity is probably related to greater cleanliness and a more healthy skin and to the wearing of clean clothing. In turn these are largely due to improved economic and social conditions, especially better houses and better food supplies.

It is desirable to have means of assessing yaws in recession. Figures such as the following are likely to be found in areas where yaws is in recession. Clinically active yaws might be found in 3–5% of patients (15% infectious, 80% keratotic, 5% late yaws). Sero-reactors without clinically active lesions would number 30–40% of all ages (50% of adults). Few clinically active cases and high sero-reactivity indicate that transmission has declined only recently, but few clinically active cases and low sero-activity indicate that transmission has not been active for a long time and conditions favouring spread from cases (which are mainly imported ones) are no longer favourable.

The author considers that the public health requirements for receding yaws can be stated thus. For small populations (or those difficult of access) and where the prevalence of clinically active yaws is more than a few cases per cent., total mass treatment (TMT), HACKETT [this *Bulletin*, 1957, v. 54, 46], is required. If the population amounts to hundreds of thousands or more, then juvenile mass treatment (JMT) should be used when the clinical prevalence is 5–10%, and selective mass treatment (SMT) when it is 2–5%. When the prevalence is under 2% all that is required is for PAM to be available at rural dispensaries for patients reporting with lesions.

There appears to be a real danger of the spread of syphilis into areas where formerly yaws gave protection but happily the incidence of syphilis in cities is probably also much lower than formerly.

[Yaws has long been recognized as a disease of the " end of the road " and it is heartening to see it receding as communications improve.]

Frederick J. Wright

LEPROSY

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

BENEDIKTSSON, G. & BJARNASON, O. Lepra i Island. [**Leprosy in Iceland**] *Nordisk Med.* 1959, Aug. 13, v. 62, No. 33, 1225–7, 1 fig.

The English summary appended to the paper is as follows:—

"Very little is known about leprosy in Iceland before the beginning of the 15th century. Thereafter the disease is thought to have been relatively common. In 1896 the number of leprous patients was 236, or 3·1 per 1,000 population. The leprous hospital was founded in 1898, and since then leprosy has declined rapidly. In 1957 there were only 8 leprous patients in Iceland among 166,344 inhabitants. Since 1937 only 2 new cases have been found, one in 1951 and the other in 1956. The latest case is reported."

VAN GORKUM, A. E. H. **Report on a Visit to Al Walid Leprosarium, Damascus, Syria.** *Leprosy Review.* 1959, July, v. 30, No. 3, 188–92.

KITANO, H. [**Epidemiological Studies on Leprosy in Gifu Prefecture. IV. Summary**] *Lepro.* 1958, Sept., v. 27, No. 5, 429–36, 3 figs. [In Japanese.]

The English summary appended to the paper is as follows:—

"Though the number of fresh cases of leprosy has decreased in recent years in Gifu prefecture, the total number of patients in the leprosarium and in private homes has increased by 21 in the past 20 years due to decrease in mortality. Including undetected cases, it is believed that there are 246 cases (1·58 per 10,000) at the present time.

"The number of non-hospitalized patients, being treated at home, have decreased by 113 in the past 20 years and there are only 24 known cases at present (0·15 per 10,000). Of these, 46% are over 60 years of age and more than 11 years have elapsed since onset in 71%. It will be a difficult problem however, to induce these patients to enter leprosaria and reduce the number of home patients.

"The small number of home patients with the L-form, the marked shift to the right in the age distribution curve both in the total number and in the fresh cases, the high proportion of cases in which 11 years or more have elapsed since onset, the type ratio (L/M+N) in fresh cases and the reduction in sex ratio, all suggest that the epidemic of leprosy in Gifu prefecture is nearing the end of its course. Gifu has reached the average level of the whole country and can no longer be considered a leprosy prevalent prefecture. It must be noted however, that the incidence of leprosy in Koreans living in the prefecture is abnormally high.

"It can be assumed that the number of undetected cases has decreased sharply due to the program of early examination and detection. It has been said that there are about 15,000 leprosy patients, including undetected cases, in Japan but it is believed that this number is too high and ca. 13,000 (1·46 per 10,000) is considered closer to the actual number."

Morris, J. A. & Nakamura, K. **Behavior of Human Leprosy Bacilli in Cultures of Human Cells.** *J. Infect. Dis.* 1959, July–Aug., v. 105, No. 1, 73–5.

Although there was no evidence that the leprosy bacilli multiplied in these tissue cultures, the authors consider that the information gained contributes to the understanding of the nature of the bacillus.

The bacilli were from subcutaneous nodules taken from cases of human leprosy in Japan and they were inoculated into the cultures within 4–6 hours of removal from the patient. The cultures were of 4 human types—intestine, liver, conjunctiva and bone-marrow. The medium (199) used for inoculation with the bacilli contained inactivated 2% horse serum or pooled human serum and it was replaced every 4–6 days; incubation was at 30–32°C. The cultures were incubated either rolled or stationary and the bacterial counts were made from standard drops on slides, prepared either with the tissue cells intact or after they had been disintegrated in a grinder.

Invasion of the cells occurred within 1–2 days and the proportion of intracellular bacilli increased for 4–5 days after which it remained stationary for 2–3 weeks and then decreased. Usually only 7–10% of the cells became infected and the number of bacilli per cell ranged from 1–38, although occasionally a cell contained 100 or more bacilli, an occurrence for which the authors had no explanation but which they considered to be worthy of further study. The use of serum from leprosy patients [the type of disease not being stated] in concentrations as high as 20% had no effect on the number of bacilli taken up by the cells, indicating that the serum contained neither a blocking nor an enhancing factor.

Serial passage of the bacilli at intervals of 14, 21, 30 and 60 days into fresh cultures showed that the bacilli continued to be taken up by the cells for 2 or 3 passages and that they persisted for 1–2 months in the new cells; bacterial counts still showed, however, no evidence of multiplication. *S. R. M. Bushby*

Bergel, M. **Influence of Various Pro-Oxidant Nutritional Conditions on the Growth *in vivo* of *M. leprae*.** *Leprosy Review.* 1959, July, v. 30, No. 3, 153–8, 4 figs. on 2 pls.

[This paper is in line with a number of previous papers on the same subject which have been abstracted in this *Bulletin*, 1958, v. 55, 172, 414, 527.]

36 male white rats were divided into 6 groups of 6 rats each. On the 21st day of age they were placed on various diets according to the group. Groups A and B were on normal diet, B being given in addition 40 to 50 mgm. of tocopherol (vitamin E) by mouth twice weekly. Group C was given a semi-synthetic diet with low content of vitamin E and 15% of crude linseed oil. Group D was given a diet similar to C with cod-liver oil in place of linseed oil. Group E had the same diet with rancid linseed oil. Group F had the deficient diet with cod-liver oil, and with 0·5 parts per 1,000 silver nitrate in its drinking water and a weekly injection of ½ to 1 cc. of rat blood haemolysate.

On the 57th day of age all the rats were inoculated into both testes with 0·1 cc. of a suspension of *Mycobacterium leprae*.

In groups A and B sections and smears from the testes showed at the 7th month only a few granular bacilli. In groups C, D, E and F there were

practically identical bacterial pictures with massive infection of the testes and other organs, but groups C and E showed the appearance of new bacilli at the 5th month, group D at the 7th month, while group F at the 5th month "showed an enormous number of strongly acid-fast bacilli, whose degree of acid-fastness was not observed in any of the other groups".

There were ceroidogenic changes in groups D and F, but it is considered that there is no connexion between this and the growth of lepra bacilli.

In general, results were more or less uniform within each group, but some animals showed fewer bacilli than others.

The particularly strong growth of bacilli in the group on rancid linseed oil suggests that there may be some connexion between the endemicity of leprosy and rancid food. "Taking into account the high variety of pro-oxidant factors and the possible combinations of two or more of these, such as for example pro-oxidant metallic catalysts, peroxides, oxygen, poly-unsaturated oils, rancid fats, irradiation, absence of anti-oxidant factors, etc., it is easy to realize that there are many possibilities for finding optimal nutritional and pharmacological conditions for the growth *in vivo* of *M. leprae*." *Ernest Muir*

OOTAKA, K., SATOO, S., SATOO, J. & MIURA, N. Une nouvelle coloration différentielle entre les bacilles de la tuberculose et les bacilles de la lèpre. [**A New Method of Differential Staining between the Bacilli of Tuberculosis and the Bacilli of Leprosy**] *Hirosaki Med. J.* 1959, Mar. 25, v. 10, No. 2, *67–*70.

The authors compare a previously described method of distinguishing tubercle bacilli from lepra bacilli by means of Sudan Black [this *Bulletin*, 1956, v. 53, 62], with their own method, and find the latter much more satisfactory. Their technique is: (1) smears are dried in the air and fixed over the flame; (2) they are covered with a 30% aqueous solution of carbol fuchsin, and after heating gently for 1 or 2 minutes are washed in water; (3) they are treated for 1 to 5 minutes with a watery solution of 5% antiformin and washed in water; (4) they are stained with Loeffler's alkaline methyline blue diluted 4 times for 30 to 60 seconds, and washed in water and dried with blotting paper. The authors found that with the Sudan Black method some of the tubercle bacilli were not stained, just like the lepra bacilli; whereas with their method the leprosy and rat leprosy bacilli were almost entirely unstained, while the tubercle bacilli were without exception stained a blue or rose colour.

Ernest Muir

SHORT, G. M. **A Further Inquiry into the Leprosy-Tuberculosis Relationship.** *East African Med. J.* 1959, June, v. 36, No. 6, 298–304. [25 refs.]

Children are born negative to tuberculin and lepromin, but most people become positive reactors to one or other or to both. How do these changes come about, and what is their significance?

The author first describes the test substances and the methods of performing the two tests. While a positive reaction to 5 TU of tuberculin denotes a previous infection with tubercle bacilli, infection with leprosy bacilli does not necessarily produce a positive lepromin reaction. Also, the lepromin reaction can be positive in people who have never had a chance of exposure to leprosy

infection; the conclusion is reached that where healthy persons react positively to small doses of tuberculin most of them also react positively to lepromin, and in the majority these results are related.

On the other hand it would appear that leprosy has little effect in stimulating tuberculin sensitivity, and it may even have a depressing effect. But when higher doses of tuberculin, up to 50 TU, are used a certain number of non-specific reactions are obtained which, among other causes, may be due to leprosy infection. 2 regions in Uganda are mentioned [this *Bulletin*, 1955, v. 52, 903; 1957, v. 54, 1419]: in Kigezi the leprosy incidence varies from 0·0 to 0·4%, and in Teso it is 6 to 8 times as great. In Kigezi, with the equivalent of 30 to 40 TU, the tuberculin index was found to be 49·63, while that in Teso was 70·88, and this in spite of the fact the population in Kigezi is far denser and therefore more conducive to the spread of tuberculous infection. It is suggested that this higher tuberculin index may be associated with the higher amount of leprosy.

It is generally assumed that tuberculous infection, as indicated by a positive reaction to 5 TU of tuberculin, produces enhanced resistance to the bacilli, though this cannot be proved since the tuberculin test cannot measure the resistance or indicate the prognosis. On the other hand the lepromin test indicates the likely course of the infection if the clinical type is in doubt. In confirmation of this the work of Dharmendra and Chatterjee is quoted: in 156 subjects who had had negative lepromin reactions 15 to 20 years before, 14·1% had developed leprosy, over two-thirds of them being lepromatous; whereas of 524 similarly placed subjects with positive lepromin reactions 15 to 20 years before, only 3·2% had developed leprosy, and none of these was of the severe lepromatous type.

The conclusion is reached that: "The leprosy and tubercle bacilli are both antigenic and allergenic. The leprosy bacillus is the weaker agent, producing an inconstant lepromin conversion and no specific tuberculin conversion; and it is in the persistently negative lepromin reactors that lepromatous leprosy, which is the reservoir of leprosy infection, develops. The tubercle bacillus is the stronger agent, producing both tuberculin and lepromin conversion and doing so in a greater number of individuals than is the case with leprosy infection. Unfortunately, this implies the replacement of one disease by, possibly, a worse. If it proves possible, as seems likely, to utilize a benign tuberculous infection, fortified perhaps by other acid-fast bacilli, to the same end, there is here an even stronger argument for the wide-spread use of BCG in tropical countries and yet another weapon in the armamentarium of the leprologist." [This valuable paper should be studied in the original.]

Ernest Muir

Silva, C. & Neto, A. V. R. Identidade do comportamento dos conviventes domiciliares de casos de lepra "indiferenciada", "tuberculoide" ou "lepromatosa", respectivamente, em face da lepromino-reação. [**Identity of Reactions to Lepromin in Subjects who had been in House Contact with, respectively, Undifferentiated, Tuberculoid and Lepromatous Leprosy**] *Bol. Serviço Nac. de Lepra.* Rio de Janeiro. 1958, Dec., v. 17, No. 4, 330–36, 2 charts.

The authors tested the lepromin reaction in 1,176 people who had been in domiciliary contact with leprosy. The results are divided according to: the

reaction (positive, doubtful and negative); age-groups (0–2, 3–6, 7–14, 15–21, 22 and over); and the form of leprosy with which they had been in contact (tuberculoid, lepromatous and undifferentiated), and these are shown in tabular form.

For the purpose of comparison these 3 factors (reaction, age, and form of disease) are plotted out in 3 graphs according as reactions are positive, doubtful or negative. In each of these 3 graphs there are 3 curves, each corresponding to the nature of the contact. In the graph showing doubtful reactions there is a period between infancy and adolescence when, in all types of contract, the proportion of reactors is low.

There are no data showing the proportions of reactors at similar ages among those who have not been in contact with leprosy. *Ernest Muir*

BERGEL, M. **Animal Lepromin with Leprosy Bacilli from Infected Rats. Preparation and Comparative Study with Human Lepromins.** *Internat. J. Leprosy.* Wash. 1959, Jan.–Mar., v. 27, No. 1, 59–67, 18 figs.

A translation, with additions, of the paper in *Semana Med.*, 1958, Aug. 7, v. 113, No. 6, 271–80, 292, abstracted in this *Bulletin*, 1959, v. 56, 449.

BROWNE, S. G. **Some Observations on the Bacteriological Index in Leprosy.** *Leprosy Review.* 1959, July, v. 30, No. 3, 174–9.

Details are given of the author's method of ascertaining the degree of infectiousness in lepromatous and dimorphous types of leprosy. For the purpose of the enquiry he examined 156 lepromatous and 34 dimorphous patients. The usual scraped incision method was used, and the following sites were examined: (1) lobe of ear, (2) forehead, (3) cheek, (4) most clinically active edge of lesion, (5) apparently healthy skin, (6) nasal mucosa. In both lepromatous and dimorphous the highest index on admission was in site No. 6 (3·54 and 2·79), and the lowest was in No. 5 (1·52 and 0·50). The various sites became negative under treatment in the order of the lowest to the highest index, the highest taking 2·26 years (lepromatous) and 1·65 years (dimorphous) on an average. The finding is stressed that often 1 or 2 sites remain positive for long periods after the other 4 sites have become negative. "The nasal mucosa, the edge of the lesion, and the ear-lobe—together account for 243 out of 280 sites last remaining bacteriologically positive." The discharge from trophic ulcers is a relatively unimportant source of infection.

Ernest Muir

IZZO, G. Attuale classificazione della lebbra e importanza della sua diagnosi precoce per la terapia. [**Current Classification of Leprosy and Importance in Treatment of Early Diagnosis**] *Acta Med. Italica.* 1958, July, v. 13, No. 7, 176–85. [46 refs.]

A general review with 2 illustrative cases.

RAMU, G. **Adult Type of Lepromatous Leprosy in a Child of 6 Months. A Case Report.** *Indian J. Child Health.* 1959, June, v. 8, No. 6, 313–14, 2 figs.

The grandfather of the child suffered from lepromatous leprosy and had a bacteriological index of 4. Macules were distributed over the buttocks, thighs

and back of the child. Smears showed separate bacilli and globi in every field. It is suggested that this is the earliest age at which this stage of the disease has been described.

Ernest Muir

WEINER, M. A. **Leprosy. Report of a Case with a Rare Histopathological Feature.** *Arch. Dermat.* 1959, June, v. 79, No. 6, 709–11, 3 figs.

"In a patient with the dimorphous (borderline) type of leprosy a rare histopathological feature was the presence of Mycobacterium leprae within intact and desquamating epidermal cells. It is suggested that this type of 'open case,' even without cutaneous or mucosal ulceration, may be an unsuspected source of dissemination of bacilli."

DE ANDRADE, L. C. & DE FREITAS, U. O tecido conjuntivo sub-epitelial na lepra tuberculoide. [**The Subepithelial Conjunctive Tissue in Tuberculoid Leprosy**] *Bol. Serviço Nac. de Lepra.* Rio de Janeiro. 1958, Dec., v. 17, No. 4, 309–22, 6 coloured figs. on 3 pls.

This work is based upon a study of 429 cases of tuberculoid leprosy. The so-called "fascia of Unna", which occurs commonly in the subepithelial layer in the lepromatous type of leprosy, is found in 15 to 18% of tuberculoid cases to take the form of an analogous disposition of the layers of tissue. In some 4% of tuberculoid cases the structure of the subepithelial fibres is identical with the "fascia of Unna" as found in the lepromatous type. In some dimorphous cases a transition can be noted, showing that the "fascia of Unna" is not a pathological condition but a phenomenon of histological accommodation. In tuberculoid leprosy there is not the change in the elastic tissue in the superficial layers that there is in the deeper tissues. Seeing that the "fascia of Unna" is present only in a proportion of tuberculoid cases, the authors suggest that possibly it depends on a difference of antigen-antibody reaction of the tissues when damaged in the various forms of leprosy. They propose to carry out further investigations.

A list is given of the various stains used in differentiating the tissues.

Ernest Muir

PRICE, E. W. **Studies on Plantar Ulcers in Leprosy. III. The Natural History of Plantar Ulcers.** *Leprosy Review.* 1959, July, v. 30, No. 3, 180–83, 9 figs. on 5 pls.

This is the third of a series of papers on this subject, in which the author describes first the pre-ulcerative stage and then the plantar ulcer.

It is important to pay attention during the pre-ulcerative stage and initiate treatment before damage occurs. The symptoms depend on the intelligence of the patient and the degree of anaesthesia. The symptoms are burning sensation, tenderness on walking, limping, cracking of a large callosity, swelling at the edge of the sole. A weekly foot inspection is important so that signs of this stage may be detected before the patient himself notices symptoms. Comparison of the two soles may show a difference between the healthy and the affected foot in its length or width or in the spread of the toes. There is

oedema of the forefoot most marked in the dorsum. On deep pressure there is tenderness. Cracks, callosities or blisters may break down into ulcers.

The plantar ulcer itself is well known ; it may be single or multiple. Plantar ulcers may be superficial or deep. In leprosy, as in diabetes, the deep ulcer has a frequent association with the neuropathic joint of Charcot, which may be at a distance from the ulcer at the tarso-metatarsal or even at the ankle joint. Superficial ulcers tend to cover a large area and may be walked on for years. The 2 determining factors are the degree of anaesthesia and the presence or absence of secondary infection. *Ernest Muir*

TARABINI, G., SOTELO, C. & CONTRERAS, F., Jr. **Two New Cases of Epitheliomas originating in Lepromas.** *Internat. J. Leprosy.* Wash. 1959, Jan.–Mar., v. 27, No. 1, 48–58, 17 figs [10 refs]

" Two new cases of epitheliomas in leprosy patients are reported. One was of the spinocellular type and the other basocellular, both developing in lepromatous skin. The clinical features of the patients are described. The histologic findings are given, with special reference to the amorphous ground substance, and also to the fibrillar elements. The observations respecting the stroma cells coincide with those of Vilanova and Rubio.

" In the study of the amorphous ground substance of the dermis, there are described zones which differ with respect to the PAS reaction, which seems to explain the greater or lesser destruction of the collagen. Qualitatively there was not seen any modification in the acid mucopolysaccharides.

" Assuming that the histochemical techniques used are good, the conclusion is reached that only the amorphous ground substance is responsible for positivity to the PAS reaction, and not the fibrillar material."

JAMISON, D. G. **An Assessment of the Effects of Outpatient DDS Administration in Katsina Province, Northern Nigeria.** *Leprosy Review.* 1959, July, v. 30, No. 3, 159–67.

This paper describes an attempt to assess the effects of DDS treatment in clinics in the Katsina Province of Northern Nigeria. Patients were examined in 7 clinics in 1957, and re-examined a year later. The number on the registers in 1957 was 2,447, in 1958 it was 2,796, and 64 patients had been discharged during the year. During the year there were 413 new patients attending of whom 314 were classified as non-lepromatous and 99 (24·2%) as lepromatous ; 99 had been removed from the register of whom 29 had died. The absentee rate had increased from 20·6% to 27·3% within the year, but in 1958 the absentee rate of lepromatous cases was only 6·0%. Of those attending in 1958 the lepromatous rate was 36·3%. Of those diagnosed as non-lepromatous in 1957 (255 cases) 9·11% were found a year later to have developed mild lepromatous characteristics, and that in spite of treatment believed to have been regularly administered.

It is remarked that the general health of patients appeared to have considerably improved because of the treatment. From the tables shown it appears that the numbers attending each clinic are increasing, and that new cases are predominantly non-lepromatous. But the development of early signs of

lepromatous leprosy in patients formerly diagnosed as non-lepromatous " indicates that the resolution of circumscribed lesions should not be regarded as a cure, since the evidence from the tables indicates that there is a real possibility of the occurrence of a lepromatous change.

" With this danger in mind it would seem that the policy adopted in Northern Nigeria of keeping leprosy patients on treatment at outpatient clinics as long as they are prepared to come has everything to commend it in our present state of knowledge." *Ernest Muir*

SATAKE, Y. [**Studies on Therapeutic Agents in Leprosy. The Effect of Acetylated DDS**] *Lepro.* 1958, Nov., v. 27, No. 6, 464–81, 23 figs. [58 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

" The majority of the therapeutic agents of the DDS series are those with an aromatic ring attached to 4-aminophenylsulfone and the amino radical in the 4 position is considered important from the standpoint of therapeutic effect. It is known that when the amino on both sides of DDS is replaced with the acetyl radical, there is a great difference therapeutically. The toxicity is reduced but at the same time the effect should also be affected. As 4,4' diacetaminodiphenylsulfone has been found to be effective against pneumococci and streptococci it can be assumed that it is converted to an effective form in the body. The mechanism of action was therefore investigated.

" Deacetylization was first studied by extracting the urine and blood of subjects given the agent with ethyl acetate and subjecting the extract to paper electrochromatography. DDS and monoacetate were proven.

" The same procedure was carried out in the DDS administered subject and monoacetate was shown to be present. Similar results were obtained with mouse liver.

" The pharmacological actions of DDS, the monoacetate and the diacetate were compared. It was found that the toxicity of the latter two was far weaker than that of DDS. It was also found that DDS paralyzes the peripheral endings of the parasympathetic nerves which accelerate intestinal motility, causes a rise in blood pressure and stops the pulsation of the toad heart in systole in a dose of 20–50 mg 20 cc whereas the latter two agents do not have these actions. On the basis of these results, it was decided that 4,4'-diacetaminodiphenylsulfone could be safely used clinically and it was applied in 10 cases of leprosy. It was found that this agent was effective. It is suggested that 4,4'-diacetaminodiphenylsulfone will be useful in cases in which DDS or Promin cannot be tolerated or in those in which there is no longer any response to Promin or DDS."

DAVISON, A. R. **The Triple Treatment of Tuberculoid Leprosy.** *Leprosy Review.* 1959, July, v. 30, No. 3, 184–5.

The triple treatment for tuberculoid leprosy consists of: (1) DDS beginning with 300 mgm. per week for the first month, and rising to 100 mgm. per day in the second month and reaching a maximum in the third month of 200 mgm. per day. (2) Trivalent antimony [this *Bulletin,* 1948, v. 45, 714] (in the form

of Fouadin or other proprietary preparation) rising from 2·5 cc. on the first day, 3·5 cc. on the second, to 5 cc. a day for 6 days a week till the patient has had 50 cc., and again after a rest of 30 days renewed, again beginning with a small dosage: if signs of intolerance arise, the 5 cc. dose is reduced to 3 cc. daily or every second day. (3) Mepacrine 200 mgm. daily for 6 days a week for 3 weeks, then renewed again after a week's rest provided there are no toxic signs.

This treatment was tried in 40 patients. "The results show that 2 females and one male still show signs of activity after 13, 10 and 11 months, respectively. The other 37 patients have become clinically cured in an average of 5 months." *Ernest Muir*

SCHNEIDER, J., LANGUILLON, J. & CLARY, J. Traitement de la lèpre par un nouveau sulfamide: la sulfaméthopyrazine. Premiers résultats. [**Treatment of Leprosy with a New Sulphonamide: Sulphamethopyrazine. The First Results**] *Bull. Soc. Path. Exot.* 1959, Jan.–Feb., v. 52, No. 1, 47–52, 11 figs. on 5 pls.

Having obtained favourable results with sulphamethopyrazine in tuberculosis, the authors made trials in leprosy. 10 leprosy patients, 6 of them with the tuberculoid and 4 with the lepromatous type of the disease, were put under treatment. The dosage was regulated so as to maintain an average blood concentration of 30 mgm. per litre. After some trials it was found that this could be maintained by administering 3 tablets of 250 mgm. each on every second day. After 11 months of trial the clinical, and in the lepromatous cases the bacteriological, results have been very satisfactory. There has been a complete absence of toxic side effects, and, surprisingly, in none of the patients has there been any sign of lepra reaction. In 1 lepromatous patient the progress was less rapid than in the others. *Ernest Muir*

DE SOUZA ARAÚJO, H. C. Caso impressionante da ineficácia das sulfonas na lepra. [**A Case suggesting Inefficacy of Sulphones in Leprosy**] *Rev. Brasileira Med.* Rio de Janeiro. 1958, Dec., v. 15, No. 12, 827–9.

The English summary appended to the paper is as follows:—

"One case of leprosy was treated during eleven years with Promin and Lyosulfon, venously, totalling more than 11 liters of both and more than 4·5 kilograms of D.D.S. Notwithstanding, he continues lepromatous and bacilliferous in the nasal secretions."

DAVEY, T. F. **Diethyl Dithiolisophthalate (ETIP or "Etisul") in the Treatment of Leprosy. A Second Progress Report.** *Leprosy Review.* 1959, July, v. 30, No. 3, 141–52, 2 figs. on 2 pls.

[For a previous report on this subject, see this *Bulletin,* 1959, v. 56, 542.] Previous observations are confirmed that diethyl dithiol*iso*phthalate [Etisul] has a marked chemotherapeutic action in leprosy, but only for 2 or 3 months. When, however, oral therapy with DDS was initiated after a short course of Etisul progress continued to be better than average.

Among 133 patients who have now been treated with Etisul there have been no signs of toxic action. In assessing progress of patients most stress has been placed on bacteriological progress, and for control purposes standard graphs of decline based upon records of progress under DDS for 10 years have been used. In 100% of milder cases, and in 70% of more severe cases there was a decline in the proportion of normal bacilli by 50% during the first 3 months when Etisul was being used alone. On the other hand a 2-month course of Etisul, given to 15 lepromatous patients with persistently positive findings under DDS treatment, produced no bacteriological results except in 2 patients.

When Etisul was given to 10 patients in combination with DDS there was a marked acceleration of reduction in the bacterial index during the first 2 months very much in excess of the DDS standard, but there was slowing down during the third and fourth months. Within 1 month of starting treatment the proportion of normal bacilli had fallen in 5 out of the 10 patients by 50%. In another group of patients who had previous DDS treatment the introduction of Etisul very much speeded up the improvement both in reducing the bacterial index and in reducing the proportion of normally staining bacilli.

When Etisul was introduced into treatment, in combination with DDS and Ciba 1906, of 15 patients, some of them with severe lepromatous leprosy, there was the same speeding up in the reduction of the bacterial index and in the decline of normally staining bacilli.

It has been found that the usefulness of Etisul has 2 aspects: the powerful chemotherapeutic action during the first 2 or 3 months, and thereafter the "continued accelerated resolution which has repeatedly been witnessed during standard chemotherapy following a short course of Etisul". With this combined treatment there have been no signs of drug resistance.

At present the most effective treatment is to begin with DDS for about a month, until the dosage of 400 mgm. weekly has been reached, then Etisul is introduced and given along with DDS up to or beyond the third month; later, Ciba 1906 may be introduced. A modification of this may be to continue Etisul as long as normal bacilli can be found in smears. After these pilot trials it is considered that large scale trials of this drug should now be begun.

Ernest Muir

JOPLING, W. H. **Corticosteroids in the Management of Foot-Drop in Lepromatous Leprosy: a Case Report.** *Leprosy Review.* 1959, July, v. 30, No. 3, 171–3, 1 fig.

An account is given of a patient diagnosed as suffering from lepromatous leprosy. While the dosage of DDS was being raised at the beginning of treatment he suddenly developed erythema nodosum leprosum and with it dropped foot. The DDS was stopped and prednisone 5 mgm. 4 times daily by mouth was given. The foot was supported in a splint at right angles except when being given passive exercises. He was given an intraneural injection of 1,500 units of hyalase dissolved in 1 ml. of 2% procaine and mixed with 1 ml. of hydrocortisone suspension (25 mgm./ml.) into the common peroneal nerve. Within a fortnight he was able to dorsiflex his foot to a right angle. Prednisone was eventually reduced to 10 mgm. daily and gradually decreased to nil in the next 2 weeks. In 8 weeks after admission the power in the affected foot was equal to that of the other side.

Ernest Muir

ELDON, J. H. **Mobile Anti-Leprosy Treatment Centres, Ghana.** *Leprosy Review.* 1959, July, v. 30, No. 3, 168–70.

BAETA, J. D. Campanha Nacional contra a lepro. Relatório de 1957. [**National Campaign against Leprosy. Report for 1957**] *Bol. Serviço Nac. de Lepra.* 1958, Dec., v. 17, No. 4, 374–94, 2 graphs.

This report gives particulars of the anti-leprosy work in 16 of the 26 Federal units of Brazil, including a population of over 44 million inhabitants of whom 35·6% have been examined. In 593 towns under control there are 10,448 patients of which 62·4% are under control. There are also 40,476 contacts with these patients who are known, and 56·4% of these are under control. Of the different forms of the disease 44·4% are lepromatous, 30·1% indeterminate, and 25·5% tuberculoid.

There are 8 work centres and 105 groups of workers, a staff of 114 leprologists and 387 doctors who are not specialists, along with 670 other workers. During the year the cost of the campaign was Cr$ 42,892,318 [about £825,000 at 52 Cr$ to £1] or about Cr$ 18·5 per patient per day. The Report dwells on the great difficulties experienced in carrying out the campaign because of the precarious means of transport, the great distances, the impact of new methods of work, and the scarcity of specialized doctors. *Ernest Muir*

CHANG, Y. T. **Evolution of Murine Leprosy.** *Amer. Rev. Tuberculosis.* 1959, June, v. 79, No. 6, 805–9, 3 figs. [12 refs.]

This report describes the disease in mice infected intraperitoneally with suspensions of omenta and pelvic pads from mice infected 5 months previously with the Hawaiian strain of *Mycobacterium lepraemurim*. The progress of the disease was measured by the number of acid-fast bacilli in the macrophages of the peritoneal exudate, the number of infected cells in the mesentery, and the bacillary populations of the spleen and the liver.

When dead bacilli were injected, there was at first a neutrophilia in the peritoneum but these cells disappeared within three weeks; the macrophages rose to 70% during the first five days and did not return to the normal level of 5% for about five weeks. The cellular response to the injection of living bacilli differed only in that the neutrophils persisted longer and the macrophages remained constant at 20–30%. The bacilli were phagocytosed mainly by the macrophages, and only occasionally by the neutrophils in the early stages. With living bacilli, the number of bacilli fell to a minimum in about 3 weeks and then increased slowly, fluctuating at a moderately low level throughout the experiment. Extracellular bacilli were rarely seen after 1 week except again at the later stages in the case of living bacilli. The response in animals inoculated with living bacilli treated with 0·01% isoniazid in the diet was similar to that in animals injected with dead bacilli, but disappearance of bacilli in the early stages was more rapid.

Mesenteric spread appeared as a thin membrane, there being a pleocytic infiltration at first but becoming dominantly macrophagic by the end of the third week. At this stage, the bacilli in the mesentery cells and the spleen had reached a constant rate of growth, whereas the rate in the liver was somewhat slower until the seventh week.

Elongation of the bacilli, a sign of active growth, was observed by the fourth

day. Their number increased steadily for 5–7 weeks and then decreased so that after 3 months the short bacilli predominated.

The average generation time of the bacilli in the spleen was 10·7 days.

S. R. M. Bushby

HIRANO, N., SUSHIDA, K. & MATSUDA, S. **Chemotherapy of Murine Leprosy. 4. The Effects of Isonicotinoyl-3,4-Diethoxybenzal Hydrazone on Murine Leprosy.** *Yokohama Med. Bull.* 1959, Apr., v. 10, No. 2, 79–82.

In a previous paper [this *Bulletin*, 1959, v. 56, 56] this hydrazone was reported to suppress the development of murine leprosy and to cause the complete disappearance of the bacilli.

The present paper describes an experiment in which this activity is confirmed. 3 mgm. of the drug given daily for 3 months to mice markedly suppressed the infection; in 10 of the 14 mice leproma did not develop from the subcutaneous injection of the *Mycobacterium lepraemurium* and in the 4 mice that developed leproma, no bacilli were found in the lesions or in the livers or spleens. Isoniazid in doses of 2 mgm. per day given to 12 similarly infected mice failed to prevent the development of the lepromas in any of the mice although the bacilli were found in only 8 of the lesions and not in any of the livers or spleens.

In a second experiment in which treatment with 5 mgm. of the hydrazone per day was delayed for 9 months, the drug again showed higher activity than 3 mgm. of isoniazid per day; none of the 9 animals treated with the hydrazone was freed of the bacilli although the bacilli were very scanty in 2 of them. The authors therefore conclude that this drug cannot be expected to have a marked effect in human leprosy. *S. R. M. Bushby*

HIRANO, N. & SUSHIDA, K. [**Chemotherapy of Murine Leprosy. 4. Isonicotinoyl-3,4-Diethoxybenzal Hydrazone**] *Lepro.* 1958, Nov., v. 27, No. 6, 485–87. [In Japanese.]

The English summary appended to the paper is as follows:—

"1) Isonicotinoyl-3-4-diethoxybenzal hydrazone (No. 284) markedly suppresses onset of murine leprosy. When treatment is continued for 3 months (3 mg daily by mouth), it becomes difficult to find acid-fast bacilli at the site of inoculation.

"2) In mice infected 9 months previously with murine leprosy bacilli and showing definite lesions, administration of 5 mg of isonicotinoyl-3-4-diethoxybenzal hydrazone daily for 2–3 months results in a macroscopic cure of the leproma or ulcer at the site of inoculation. Acid fast bacilli, however, are still present. When treated with INH (3 mg daily *per os*), acid fast bacilli were found not only at the site of inoculation but also in the liver and spleen."

[For references to earlier parts, see this *Bulletin*, 1959, v. 56, 56.]

NISHIMURA, S., KOSAKA, K. & YASUKAWA, T. [**The Effect of Cycloserine in Murine Leprosy**] *Lepro.* 1958, Nov., v. 27, No. 6, 493–5, 1 chart. [In Japanese.]

The English summary appended to the paper is as follows:—

"Cycloserine was administered in a dose of 1·0 mg daily, 6 days a week for

120 days in mice inoculated with a small quantity or large quantity of murine leprosy bacilli and the effect compared to that in the untreated control.

" No effect was noted in the groups inoculated with either the small or large quantity of bacteria and no difference due to the dose of cycloserine was found. In other words, there was no difference between the treated group and the untreated control. From the results, it is believed that this agent has no effect in murine leprosy.

" The results differ from those of Chang [this *Bulletin*, 1958, v. 55, 1132], but this may be attributed to the difference in experimental methods. A universal standard screening method should be set up as soon as possible."

HELMINTHIASIS

*In this section abstracts are arranged as far as possible in the following order:—*TREMATODES *(schistosomes, other flukes);* CESTODES *(Diphyllobothrium, Taenia, Echinococcus, other cestodes);* NEMATODES *(Hookworms, Ascaris, Filarial worms, Dracunculus, etc., Trichuris, Enterobius, Trichinella, etc.).*

PESSÔA, S. B. Considerações sôbre as verminoses no Nordeste brasileiro. [**Helminthiasis in North-Eastern Brazil**] *Rev. Inst. Med. Trop. São Paulo.* 1959, May–June, v. 1, No. 1, 57–80, 2 figs. [96 refs.] English summary.

This is an immense region and the report refers to findings in 7 States. Examination of 173,537 schoolchildren in 1950 gave the following percentage infections: — *Ascaris* 86%, *Trichuris* 52%, *Ancylostoma* spp. 47%, *Strongyloides stercoralis* 8·5%, *Schistosoma mansoni* 10·7%, cestodes spp. (*Taenia* and *Hymenolepis nana*) 0·5%. The people are very poor and undernourished with a diet especially deficient in protein and vitamin A; hygienic measures are almost non-existent; and the soil, water, and air [see below] are contaminated. Under these conditions it is easy to see how such heavy infections can exist. In one place, out of 496 persons aged 9 to 60, *S. mansoni* was found in 40·7% and *Ancylostoma* spp. in 55·6%.

As an indication of how children become infected at a very early age, it is shown that *S. mansoni* was present in 1·6%, *Ascaris* in 60%, and *Ancylostoma* spp. in 18·7%, of 181 children under 1 year old, and a baby only 45 days old was found with an *Ascaris* infection.

As an example of how ova can be disseminated by the wind, the authors exposed microscope slides covered with cedar oil for 2–3 days behind the laboratory in the centre of the city of Aracaju and found as many as 70 *Ascaris* ova on 1 slide. In the endemic areas schistosome infection is usually acquired at an early age. Here the authors point out that the most serious sites for infection are pools near houses where the snail vector (*Australorbis glabratus*) is present in large numbers.

Among general measures for prevention they suggest protein supplementation, *e.g.*, by cheese, dried casein, etc.; also that schoolchildren be given anthelmintics once each year. In conclusion they emphasize that the problem of helminth infections in the 7 states studied is less medical than socio-economic, though the gravity of *S. mansoni* endemicity cannot be over-emphasized.

[It is understood that recently a focus of *S. mansoni* infection has been found

near Fordlandia. However, the general problem alone is so vast as to make even the stoutest heart quail. The southward spread of the snail vector may even be favoured by the great hydro-electric works now under construction.]

W. K. Dunscombe

VINKE, B. & VAN DER SAR, A. Ervaringen met dithiazanine, een nieuw wormmiddel. [**Dithiazanine, a New Vermifuge**] *Nederl. Tijdschr. v. Geneesk.* 1959, July 18, v. 103, No. 29, 1477–8.

The English summary appended to the paper is as follows:—

"Dithiazanine, a new anthelmintic with broad-spectrum activity, was tried in 76 patients with 100 worm infections. The drug seems valuable, although the side effects, such as vomiting (33 per cent.) and diarrhoea (3 per cent.) make it impracticable for use in some cases."

[For other references, see also this *Bulletin*, 1959, v. 56, 1039.]

AMARAL, A. D. F., PIRES, C. D. de A., AMATO NETO, V., FERREIRA, C. S. & FERREIRA, J. M. Observações sôbre a atividade anti-helmíntica da ditiazanina. [**The Anthelmintic Activity of Dithiazanine**] *Rev. Inst. Med. Trop. São Paulo.* 1959, May–June, v. 1, No. 1, 41–56. [13 refs.] English summary.

This investigation was aimed at testing the activity of dithiazanine [this *Bulletin*, 1959, v. 56, 1039] on *Strongyloides stercoralis, Trichuris trichiura, Ancylostoma* spp., and *Schistosoma mansoni.* 15 prisoners from the State penitentiary at São Paulo were examined for intestinal helminths by 5 methods, and 15 out-patients including 3 children aged 12 years or less were examined by 4 methods. 13 of the prisoners had also duodenal intubation before and after treatment.

Dithiazanine was given as enteric coated tablets of 100 or 200 mgm. thrice daily in various schemes of treatment, varying from amounts of 1200 mgm. in 3 days (with no *S. mansoni* present) to as much as 12,600 mgm. in 21 days.

The results showed that the drug was completely satisfactory for *S. stercoralis,* all 20 positive patients being cured. 11 out of 14 patients positive for *T. trichiura* were also cured but on ankylostome and schistosome infections the drug was ineffective. 1 of 4 *Ascaris* infections was cured. Symptoms of intolerance were present in most of the patients especially at the beginning of treatment. These were nausea, vomiting, abdominal pains, and diarrhoea. In 2 cases treatment had to be stopped but no evidence of liver damage was found.

W. K. Dunscombe

VORA, D. D., JUNNARKAR, V. K. & VELAME, V. P. **Experimental Study of Concentration of Oxygen during its Absorption in Small Intestine.** *Indian J. Med. Sci.* 1959, June, v. 13, No. 6, 481–5.

"The concentration of oxygen in small intestine of dog under experimental conditions varies from 84% to 90% at the end of first hour. This points to the fact that the anthelmintic action of oxygen is definitely being exerted, in live animal, during first hour. Whereas, during second hour, though the concentration of oxygen varies from 70% to 81%, the amount of oxygen that remains

unabsorbed is variable over a wide limit, hence the anthelmintic action during second hour is not predictable."

JANZ, G. J. & DE CARVALHO, A. M. Nota preliminar sobre a existência de bilharziose mansoni no Alto Zambeze (Angola). [**The Existence of** *Schistosoma mansoni* **Infection in Upper Zambesi, Angola; Preliminary Note**] *Anais Inst. Med. Trop.* Lisbon. 1957, Sept.–Dec., v. 14, Nos. 3/4, 377–81.

The English summary appended to the paper is as follows:—

"The authors mentioned the recent discovery of autochthonous cases of bilharziasis by *Sch. mansoni* in the circumscription of 'Alto Zambeze' (Moxico, Angola). The investigations gone through with 'Missão de Prospecção de Endemias' in Angola, in the North Angola frontier (Cabinda and Congo) did not show the existence of the illness in that region."

DE MORAIS, T. As bilharzioses humanas no distrito de Moçambique (A.O.P.). [**Human Schistosomiasis in the District of Mozambique**] *Anais Inst. Med. Trop.* Lisbon. 1957, Sept.–Dec., v. 14, Nos. 3/4, 461–70, 1 graph.

The English summary appended to the paper is as follows:—

"In the Moçambique district both intestinal and vesical bilharziasis were found. *Schistosoma haematobium* is more or less homogeniously widespread and *Schistosoma mansoni* patchily distributed. In 980 examinations done in children from 3 to 16 years of age 80·91% were found to be infected by *Schistosoma haematobium* and 6·42% by *Schistosoma mansoni*.

"It does not seem that age and sex have any influence in the incidence index of both forms of the disease. Altitude although not influencing *haematobium* infections shows a definite tendency to reduce the degree of infection by *mansoni*. *Schistosoma mansoni* was not found in altitudes over 1000 meters."

DE MORAIS, T. As bilharzioses humanas no distrito de Cabo Delgado (A.O.P.). [**Human Schistosomiasis in Cape Delgado District, Mozambique**] *Anais Inst. Med. Trop.* Lisbon. 1957, Sept.–Dec., v. 14, Nos. 3/4, 455–60, 1 map.

The English summary appended to the paper is as follows:—

"Of 740 examinations done in Cabo Delgado 67·83% were positive to the presence of *Schistosoma haematobium* in urine.

"The same number of stool examinations did not show the presence of *Schistosoma mansoni*.

"There does not seem to be any relation between the degree of infection and the sex or age of the children examined.

FRAGA DE AZEVEDO, J., GÂNDARA, A. F. & FERREIRA, A. P. Sobre a presença da bilharziose vesical não autóctone na Província de Timor. [**Vesical Schistosomiasis (Non-Autochthonous) in Timor**] *Anais Inst. Med. Trop.* Lisbon. 1958, Mar., v. 15, No. 1, 259–62.

The English summary appended to the paper is as follows:—

"Some vesical bilharziasis cases were verified in Melanoafrican soldiers who were temporarily stationed at some places of Portuguese Timor.

"In two of these places in 113 and 149 persons, of whom 105 and 96 were adults, no autochthonous case was revealed.

"The conditions are probably favourable for the development of infections such as bodies of water, vector molluscs and the life of the population."

BRYGOO, E. R. & RANDRIAMALALA, J. C. Différence de colorabilité au Ziehl entre les oeufs de *Schistosoma mansoni* et ceux de *Schistosoma haematobium*. [**Difference in Ziehl-Neelsen Staining between Eggs of** *Schistosoma mansoni* **and of** *S. haematobium*] *Bull. Soc. Path. Exot.* 1959, Jan.–Feb., v. 52, No. 1, 26–7.

The authors, from the Pasteur Institute of Madagascar, confirmed the finding by LICHTENBERG and LINDBERG [this *Bulletin*, 1955, v. 52, 551] of an acid-alcohol-fast substance in the capsule of the egg of *Schistosoma mansoni*.

They have studied this staining reaction in tissue sections fixed in Bouin's fluid and treated with lithium carbonate to remove the picric acid: the preparations were then re-acidified in N/10 HCl for 1 minute. Staining by the Ziehl-Neelsen method was carried out in the cold for 30 minutes.

While constant results were obtained with eggs of *S. mansoni*, those of *S. haematobium* were always negative. Eggs of both species, from faeces and urine respectively, were embedded side by side in paraffin so that they could be compared on one slide. The *S. mansoni* were seen to retain the bright red colour while those of *S. haematobium* had lost it.

The authors point out the practical value of this phenomenon for differential diagnoses, especially in scanty infections (in 16 sections containing schistosome eggs in 1958, they were able to make a specific diagnosis on morphological grounds in only 6 cases).

Apart from this the findings are of interest in relation to the chemical constitution of the eggs of the two species. *H. J. O'D. Burke-Gaffney*

HERVE, A. & PIGANIOL, G. Donnés récentes dans la bilharziose urinaire. [**Recent Observations on Urinary Schistosomiasis**] *Anais Inst. Med. Trop.* Lisbon. 1958, Sept., v. 15, No. 3, 647–77.

The authors have studied 100 male patients [presumably Africans in Portuguese territory] suffering from urinary schistosomiasis, paying particular attention to the following:—

(1) endoscopy of the bladder and study of its histology;
(2) intravenous pyelography;
(3) male genital complications, with radiography of the seminal vesicles and vas deferens after surgical exposure and the injection of diodone in 13 selected patients;
(4) stone formation, and its relation to crystalluria.

The findings, under these various headings, are listed and are compared and contrasted with those recorded by other workers in this field. The details should be sought in the original by those interested. Worthy of note is a description of "black microgranulations" due to altered blood pigment, which are said nearly always to be seen cystoscopically in those patients suffering from a microscopic haematuria. Upper urinary tract lesions, with ureteric

damage and hydronephrosis, were found in 27 patients; 18 of them were bilateral. The authors considered that 22 of these were attributable to stenosis of the ureteric orifices; 5 of them were ascribable to an atonic dilatation of the ureters. Surgical ureteral dilation was effective in relieving 3 of the authors' patients; plastic operations with transplants were done in 3 others, and gave spectacular immediate relief though later resultant complications followed. As the effect of such lesions is progressive, when surgical intervention is deemed desirable it should not be delayed.

Urethritis, epididymitis, seminal vesiculitis, or prostatitis were seen in 21 patients. A reactionary hydrocoele may mark schistosomal epididymitis, and differential diagnosis from tuberculous disease may not be easy; both conditions were found concurrently in one patient. The seminal vesicles were involved in 7 of the 100 patients, the prostate in only 2.

Calcification was seen in the bladders of 18 patients, and in the ureters of 2; there was a pelvic calculus in one case, and calculus formation around a fragment of a sound left in the bladder of another. The authors' experience of the incidence of urinary calculus formation accords with that reported in Africans in Rhodesia, and not with that in Egypt where it is said to be much more frequent.

Patients with urinary schistosomiasis, most of whom suffer from pyuria and whose bladders cannot retract fully, appear to offer every opportunity for urinary stone formation. Urinary excretion studies in Africans suffering from this form of schistosomiasis show that they tend to pass urines of low specific gravity which are usually acid and commonly contain some phosphate, oxalate or urate crystals, though not an excessive amount of these. The slight tendency to stone formation among them is probably a racial characteristic; it also may be related to the presence of protective colloids in the urine of the African.

A. R. D. Adams

Ishak, K. G. & Abdel Malik, I. K. **Schistosomiasis of Spleen with Abscess Formation and Infarction.** *Amer. J. Trop. Med. & Hyg.* 1959, May, v. 8, No. 3, 319–23, 5 figs.

Reports of actual parasitic involvement of the spleen in cases of schistosomiasis are few. The authors treated a 23-year-old male Egyptian who had suffered from a painful and tender swelling in the left upper abdomen for 2 months, associated with fever, anorexia, headache and drowsiness. He gave a history of haematuria in childhood, and of haematemesis 3 years before the present trouble. He was acutely ill, wasted and pallid, with clinical evidence of cor pulmonale. The swelling was irregular and extended down to the umbilicus; its border was rounded and a notch could be felt. The liver was enlarged 3 fingers and firm; there was no ascites. The blood picture was normal but for a marked hypochromic anaemia; no schistosome eggs were found in the stools or urine; the latter also was otherwise normal. Radiography of the chest showed raising and fixation of the left diaphragm; the lung appearances were consistent with cor pulmonale.

At operation a large adherent spleen was found to contain 1 litre of yellow pus and much necrotic tissue; the whole organ was removed and the patient 4 years later is in good condition. The upper pole of the spleen was necrotic and separated from the rest of the organ. Other necrotic areas were found in

the body of the spleen, the capsule of which was uneven and thickened, with many fibrous adhesions; the trabeculae also were thickened. There was much fibrous tissue and vascular granulation tissue with recent arterial thrombus formation and infarction in the pulp, which also contained many schistosomal granulomata. Haemosiderin granules were abundant, as were inflammatory cells—chiefly plasma cells. Many *Schistosoma haematobium* and *S. mansoni* eggs, mostly non-viable, were found in the granulation tissue. No adult worms could be seen in the splenic vein or its branches; eggs were seen within the walls of a large trabecular artery; this suggested their arrival by embolus through the splenic artery from the pulmonary circulation. The escape of these eggs from the pulmonary into the systemic circulation by arterio-venous fistulation in pulmonary schistosomiasis, or through normal arterio-venous fistulae, has been postulated by other workers [*e.g.*, this *Bulletin*, 1952, v. 49, 634; 1957, v. 54, 310]. The authors regard the condition of this patient as attributable to chronic pulmonary schistosomiasis, with cor pulmonale; probably hepatic schistosomiasis with portal hypertension and oesophageal varices; and fibrocongestive lesions of the spleen before the embolism occurred. The reason for gross splenic abscess formation is not clear. *A. R. D. Adams*

Brink, C. J. H., Botha, H. P., Combrink, H. J. & Erasmus, F. J. **Mass Chemotherapy in Bilharzia in Northern Transvaal.** *South African Med. J.* 1959, June 27, v. 33, No. 26, 536–42, 1 map & 2 figs. [29 refs.]

Surveys of Bantu schoolchildren in the subtropical parts of the Northern Transvaal show that over one-half of them have schistosomiasis. *Schistosoma haematobium* infection alone is found in the major part of the 60,000 square mile territory north of Pretoria; both it and *S. mansoni* infection are about equally prevalent in the Eastern side to a depth of about 100 miles. The Bantu population in these areas is some 1½ million. Economic development with better cultivation and extended irrigation favour the spread of the parasites; malaria in these areas has now largely vanished. In addition to schistosomiasis hookworm infection was found in 14% of the schoolchildren examined, *Ascaris* in 10·5%, and tapeworm in about 1%. Though in theory schistosomiasis should be readily controllable by treatment of disclosed cases, by snail control, by proper sanitation, by the provision of suitable domestic water supplies and by educational campaigns, in practice these are not easy to achieve; the measures to solve it so far applied here have been costly and inadequate. Initial surveys at various schools throughout the area have shown that the epidemiological picture varies much from region to region. In spite of the high incidence of schistosomiasis in the children clinical ill-health has not been found to be attributable to it on a material scale; the school attendance figures of infected children are good and their physical condition remains good even when they are passing blood in the urine or faeces. The authors think that schistosomiasis is only a section of the wider problem of helminthiasis, and incline to the view that it is not necessarily a very important one.

Treatment of comparable groups with Nilodin (Borroughs Wellcome) or with Miracil D Co. (Bayer), and a control group with Blaud's pill, over a period of a normal school week was disappointing; the infection rates in the 3 groups were not statistically affected. Snail control by copper sulphate applications on an

adequate and effective scale proved impracticable. Educational campaigns to promote sanitary habits and to avoid infection are making only very slow progress; they need reinforcement by general practitioners and the lay public. A very much more vigorous effort must be made if schistosomiasis is ever successfully to be combated in S. Africa, but more promising evidence must be forthcoming that better results at a reasonable cost can be achieved than those here recorded before the effort can be expected. *A. R. D. Adams*

CORREA, R. R., CODA, D. & OLIVEIRA, U. A. Um foco autóctone de esquistossomose no Vale do Paraíba. Nota previa. [**An Autochthonous Focus of Schistosomiasis in the Paraíba Valley, Brazil**] *Folia Clin. et Biol.* S. Paulo. 1956, July–Dec., v. 26, Nos. 1/6, 85–90, 3 figs. & 1 map. [17 refs.]

The English summary appended to the paper is as follows:—

"1 — Five autochthonous cases of schistosomiasis mansoni were found in Pindamonhangaba, a town situated on the Valley of Paraíba, State of São Paulo, Brazil.

"2 — 506 planorbidae of the species *Australorbis nigricans* (Spix, 1827) were collected and 498 out of them were examined and 1 (0·20%) was naturally infected with cercariae of *S. mansoni*.

"It is believed that this was the first time that *A. nigricans* was found infected on the plateau of the State.

"The breeding-places were ditches the waters of which are contaminated by human feces."

PELLEGRINO, J.; BRENER, Z.; DA SILVA, J. F. Estudo comparativo entre a reação intradérmica e o exame de fezes no diagnóstico da esquistossomose mansoni. I. Observações feitas em crianças residentes em foco de alta endemicidade [PELLEGRINO, BRENER & DA SILVA] [**Comparison between the Intradermal Test and the Results of Faecal Examinations in *S. mansoni* Infections. I. Observations on Children resident in a highly endemic Area**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1958, July, v. 10, No. 3, 291–6. English summary. II. Observações feitas em adultos [PELLEGRINO & BRENER] [**II. Observations on Adults**] *Ibid.*, 297–302. English summary.

These reports deal with comparison of the intradermal (ID) test and the results of faeces examinations by the Hoffman, Pons and Janer method in *Schistosoma mansoni* infections at Belo Horizonte, Brazil.

i. 454 pupils aged 10–15 years at an agricultural school were tested. Large numbers of infected *Australorbis glabratus* were found near by. The ID antigens were made up from dried cercariae, or adult *S. mansoni*, and an amount of 0·05 ml. was injected into the flexor surface of the forearm, a 12 mm. diameter weal being taken as positive. Comparing a *single* faeces examination with the ID reactions, the results were: faeces 298 +, cercarial antigen 262 +, adult schistosome antigen 250 +, and with both antigens 289 +. In a number of children ova of *S. mansoni* were not found until the fifth faecal examination, while in 61 patients positive with the ID test and

with negative faeces tests, ova were finally found in 52. There was no significant difference between the 2 antigens.

The results suggest that faecal examination is best for diagnosis; that in patients ID positive and faeces negative, repeated faecal examinations are necessary; that simultaneous faeces and ID tests are advantageous.

ii. 558 members of a battalion of Military Police were tested with similar antigens to those above, the 12 diameter weal again being taken as positive. In contrast to tests with children, these tests showed faeces 135 + but ID 299 + to one or both antigens, and comparison of the antigens in 558 specimens gave 94% agreement. In 174 of 182 men with a positive ID test and whose first faeces specimen was negative, repeated faeces examination gave 112 positive, and another 2 others were positive by rectal biopsy. There were also 8 who had had positive faeces before the study and 3 who had been treated. In 45 men ID + but whose faeces were repeatedly negative the complement-fixation test with an adult schistosome antigen was + in 22. Thus out of 174 men ID + whose first faeces specimen was negative, 147 eventually showed evidence of a schistosome infection.

The authors conclude that (1) the ID test is of value in cases where faeces are negative as it indicates that further examinations are required; (2) the ID test is more sensitive in adults than in children; (3) there is no easy explanation of those ID positive cases where repeated faeces examinations and also the complement-fixation test are negative, though extinct or unisexual infections or even false positives may be possible explanations. *W. K. Dunscombe*

Barbosa, F. S., Coelho, M. V. & Coutinho-Abath, E. Infestação natural e experimental de alguns mamíferos de Pernambuco por *Schistosoma mansoni*. [**Natural and Experimental Infection of Various Mammals with** *Schistosoma mansoni* **in Pernambuco, Brazil**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1958, Apr., v. 10, No. 2, 137–44. [28 refs.]

The English summary appended to the paper is as follows:—

"Natural infection of *Cavea aperea aperea* with *Schistosoma mansoni* is reported for the first time from Northeast Brazil. Experimental infections of several mammals are reported. The anteater, *Tamandua tetradactyla*, and a wild rat, *Cercomys cunicularis laurentius*, not yet listed as potential hosts of the trematode, were successfully infected. The infected animals were submitted to parasitological and histological examination."

Robinson, E. J., Jr. **Recovery of** *Schistosoma mansoni* **from Hormonally Imbalanced Hosts.** *Exper. Parasit.* New York. 1959, June, v. 8, No. 3, 236–43.

"1. Experiments are described in which male mouse hosts of *Schistosoma mansoni* were castrated, injected with testosterone, or subjected to these treatments simultaneously, and the survival rates of the worms compared to those of controls.

"2. Certain effects of the experimental treatments are described, but they were not consistently obtained, and differed from others reported.

"3. It is concluded that the possibility exists of changing the survival rates

of schistosomes by disturbing the hormonal balance of the hosts, but that all the conditions required for a predictable change are not known."

[See this *Bulletin*, 1958, v. 55, 548.]

DUSANIC, D. G. **Histochemical Observations of Alkaline Phosphatase in** *Schistosoma mansoni*. *J. Infect. Dis.* 1959, July–Aug., v. 105, No. 1, 1–8, 8 figs. [18 refs.]

MAO, Ying-Chi, SHENG, Shun-Chiüng, TU, Ch'i-K'uei, FANG, Jung-Ch'üan, FANG, K'un-Yen, SHEN, Jo-Se, CHOU, Shu-Nü & HUANG, Chin-Yuan. **Oral Tartar Emetic Treatment of Schistosomiasis japonica.** *Chinese Med. J.* Peking. 1959, June, v. 78, No. 6, 532–41.

Some 3,000 patients, of all ages from 5 years and of each sex, suffering from different stages of *Schistosoma japonicum* schistosomiasis have been treated in Chekiang with tartar emetic given orally. In general the drug given by this route was well tolerated; the patients could therefore be dealt with as out-patients; and the immediate and the later results of the treatment proved remarkably satisfactory. This paper records data concerning 556 of these patients.

The drug used was potassium antimony tartrate to which was added an equal amount of sodium bitartrate; the mixture was given in enteric coated capsules or tablets, each containing 10 to 50 mgm. For adults 30 mgm. was given in 3 doses on the first day; 60 mgm. similarly on the second day; 150 mgm. on the third day; and then 300 to 450 mgm. daily in divided doses, the largest dose of the 3 being in the evening, to a total of 100 to 120 mgm./kgm. body weight. Relevant data are set out in a number of tables. Debility, nausea, vomiting, anorexia and dizziness were the most frequent side-effects and occurred in up to one-third of those treated; abdominal pain and distension were rather less common; other side-effects were of low incidence. The capsules were less satisfactorily tolerated than were the tablets; the amount of enteric coating probably had a bearing on this. The average duration of treatment was 17·2 days; when reaction was severe the dosage was reduced or, if necessary, suspended for some days; children and peasant farmers withstood the treatment best, students much less well. Reactions were most apparent in the middle of the course of treatment; they lessened towards its end. 98% completed the full treatment, and most of these were observed for months or up to 2 years afterwards. Quantitative studies of the blood and urine antimony levels showed these to reach their peak about the 16th day of treatment. The authors do not attach undue importance to these figures, as it is antimony in the form of tartar emetic which is schistosomicidal.

The immediate results of treatment were the disappearance of "cercariae" [*sic*] from the stools [obviously a miracidial hatching test], and betterment in the clinical condition of the patients with reduction in the sizes of the liver and spleen, and in the amount of ascites and dysentery. The immediate therapeutic response was assessed at 90%; this declined to 60% on later re-examinations.

The authors state that the addition of sodium bitartrate to the tartar emetic delays the decomposition of the latter, in the gastric juice and the intestinal

juices, into an acid of antimony and antimony oxide which are non-absorbable precipitates; this delay facilitates the absorption from the bowel of the tartar emetic, which is the therapeutically active agent. Tartar emetic if effective when given by mouth possesses great advantages, not only in the method of administration and all that this entails but in its safety and the savings in cost gained by oral out-patient treatment.

[This work, if confirmed, is of major importance in view of its implications.]

A. R. D. Adams

SUN, Qi-Xun, CHEN, Wei-Zhou, LI, Hsiao-Yü & TING, Kuang-Sheng. [**Studies on Antischistosomal Drugs. XV. Effect of Tartar Emetic on the Cerebral Blood Flow in Rabbits**] Reprinted from *Acta Physiologica Sinica*. 1959, June, v. 23, No. 1, 29–36, 4 figs. [19 refs.] [In Chinese.] English summary.

HAMADA, M. [**Studies on Experimental Paragonimiasis**] *Shikoku Acta Med.* 1959, Mar., v. 14, No. 3, 417–38, 30 figs. on 5 pls. [73 refs.] [In Japanese.] English summary.

The author, from Tokushima University School of Medicine, Japan, studied the host-parasite relationships of *Paragonimus westermani* infection in dogs infected experimentally and killed 20 to 210 days later.

Histochemical studies were made of the lung lesion and of the adult worms taken from the lung cysts in the 5th month. The histological changes in the lung and the chemical changes in the fluke were also studied after emetine treatment.

Lung invasion by the fluke was seen after 23 days. Up to the 35th day, catarrhal pneumonia and bronchitis were seen about the site of infection: thereafter chronic interstitial pneumonia and cyst formation were observed. The changes then became localized with little invasion. Parallel with the chronic changes and cyst formation, proliferation of lattice and collagen fibres became prominent, while elastic fibres around the cyst in the lung decreased and never proliferated at any stage.

Up to 35 days after infection, a notable increase of phosphatase and decrease of polysaccharide and nucleic acid occurred. These changes reversed after 40 days and almost normal levels were reached after 90 days. In bronchi close to the fluke cysts, the phosphatose reaction was strongly positive even after 210 days. Glycogen was present in the largest amounts in the reticular tissue, vitelline gland, sucker and pharynx of the fluke, and in smaller amounts in the subcuticular layer and ovary: none was found in the intestine and testis. Other polysaccharides were found in the intestine, vitelline gland and ovary. Acid phosphatase was detected in most of the organs, especially in the intestinal epithelium, and alkaline phosphatase only in the excretory organ. RNA and DNA were most dense in the testis, ovary and vitelline gland, relatively dense in the intestinal epithelium and sporadic in the subcuticular layer, sucker and pharynx.

In dogs benefiting from emetine, there was marked hyperaemia of the blood vessels in the wall of the fluke cyst and noticeable bleeding in the surrounding lung tissue. The killed fluke was absorbed completely 40 days after treatment was begun.

During emetine treatment, there was a striking decrease of glycogen in the reticular tissue and subcuticular layer of the fluke, a decrease of acid phosphatase in the intestinal epithelium and subcuticular layer and a decrease of nucleic acid in the vitelline gland, ovary and testis; this suggests that these substances play a prominent part in maintaining the life and reproductive function of the fluke. *H. J. O'D. Burke-Gaffney*

MANSOUR, T. E. **Studies on the Carbohydrate Metabolism of the Liver Fluke** *Fasciola hepatica. Biochim. et Biophys. Acta.* 1959, Aug., v. 34, No. 2, 456–64, 2 figs. [16 refs.]

EPSTEIN, E., PROCTOR, N. S. F. & HEINZ, H. J. **Intra-Ocular Coenurus Infestation.** *South African Med. J.* 1959, July 18, v. 33, No. 29, 602–4, 3 figs. [16 refs.]

" A case of intra-ocular infestation with a coenurus of *Multiceps multiceps*, and its successful removal, is described. Aspects of intra-ocular helminthic infestation and the relation to the diagnosis of pseudo-tumour are discussed. The value of exploratory sclerotomy is suggested."

[See this *Bulletin*, 1957, v. 54, 321, 322, 1333.]

AGOSIN, M. & ARAVENA, Luisa. Enzimas del ciclo de las pentosas en *Echinococcus granulosus*. Comunicaciòn preliminar. [**Enzymes of the Pentose Cycle of** *Echinococcus granulosus*] *Bol. Chileno de Parasit.* 1959, Apr.–June, v. 14, No. 2, 30–33, 6 figs. [10 refs.]

The English summary appended to the paper is as follows:—

" Cell-free extracts of scolices of *Echinococcus granulosus* have been shown to possess several of the enzymes of the hexose monophosphate oxidative route or a very related one. Whether this system is operative *in vivo* remains to be established."

ARMAND UGÓN, C. V. Hidatidosis pulmonar bilateral. [**Bilateral Pulmonary Hydatidosis**] *Archivos Uruguayos de Med., Cirug. y Especialidades.* 1958, Sept.–Oct., v. 51, No. 5, 462–5, 3 figs.

A case in a Brazilian boy of 9.

MORA LOPEZ, J. Quiste hidatidico de Bazo. Comentarios sobre un caso. [**Hydatid Cyst of the Spleen**] *Maroc Méd.* 1959, May, v. 38, No. 408, 706–14, 2 figs. [24 refs.] French summary.

A case from Tetuan, Spanish Morocco.

HAAS, H. G. & RÜTTNER, J. R. Echinococcus alveolaris der Leber mit Metastasierung in die Lungen. [**Alveolar** *Echinococcus* **Infection in the Liver with Metastases in the Lungs**] *Schweiz. med. Woch.* 1959, Aug. 1, v. 89, No. 31, 813–17, 6 figs.

CASTILLO LINDLEY, E. La metoquina en las teniasis. Experiencia con 686 casos. [**Metoquine in Taeniasis. A Study of 686 Cases**] *Rev. Sanidad Policía.* Lima. 1958, Dec., v. 18, No. 6, 545–56.

The author, from Lima, Peru, treated 686 patients suffering from taeniasis and aged from 1 to 73 years by means of metoquine [mepacrine] during the last 10 years.

In this paper, he describes the study and results and also some *in vitro* experiments on various helminths, together with studies of the effect of metoquine on the nervous system of crustaceans: these last studies were not conclusive, but the *in vitro* studies did suggest that the paralysis and death of the worms were hastened when the *p*H of the metoquine was adjusted with sodium bicarbonate. [The interpretation of these experiments is limited by the fact that although there are references in the text to "tables 1 to 9," in fact only table 1 is printed.]

In the clinical studies, 8 regimes were used in which such factors as diet, purgation, administration of the drug and timing were varied. The dose of metoquine varied from a single tablet of 0·1 gm. per year of age in children under 4 years to 8 or 9 such tablets in persons over 17 years.

The regime found most satisfactory was as follows: the patient had an exclusively milk diet on the day before treatment and a saline purge that night, and the next morning he received 1 tablet (0·1 gm.) of metoquine on an empty stomach; this dose was repeated every 5 minutes until he had received the total dose according to age. The tablets were taken with a solution of sodium bicarbonate. Four hours after the last dose, the patient received a purgative of castor oil.

After a control period of at least 3 months 659 (96%) of patients were adjudged cured and of these 70% passed the scolex.

A number of side-effects were observed, notably nausea (60%), vomiting (44%), headache (26%). On the whole, these reactions responded readily to appropriate treatment. One patient developed an alarming mental condition after 3 days.

The author considers that there are certain contra-indications to the use of the drug, especially the presence of liver or kidney ailments, acute intestinal lesions, mental conditions and pregnancy.

He finally concludes by recommending the use of metoquine in the treatment of cestode infections. The *in vitro* studies, which were carried out with earthworms and various cestodes obtained from domestic animals, suggested that the drug was less effective against nematodes because of their thicker protective cuticle. *H. J. O'D. Burke-Gaffney*

CHHUTTANI, P. N. & CHUGH, K. S. **Hookworm Disease in the Punjab.** *J. Ass. Physicians India.* 1959, July, v. 7, No. 4, 327–31, 2 figs. [14 refs.]

"Hookworm disease commonly seen at Patiala was studied in 50 patients to assess the intensity of infestation and identify the species of worms. It was found that 19 harboured on an average 135 or more worms per patient. Statistically significant positive correlation was demonstrated between the egg count and number of worms. Similarly a significant negative correlation was demonstrated between the haemoglobin and the number of worms harboured. A total of 4143 hookworms was identified to be all *Ankylostoma duodenale*."

ROCHE, M., PÉREZ-GIMÉNEZ, María E., LAYRISSE, M. & DIPRISCO, Estela. Hemorragias gastro-intestinales en la infestación con anquilostoma. [**Gastro-Intestinal Haemorrhage in Hookworm Infection**] *Archivos Venezolanos de Nutrición.* 1957, Dec., v. 8, Nos. 1/2, 39–55, 5 figs. [12 refs.] [Published in English in *Amer. J. Digestive Dis.* 1957, May, v. 2, No. 5, 265–77.]

The English summary appended to the paper is as follows:—

"Five cases of hookworm infection associated with anemia have been presented in which intestinal blood loss seemed to be a major causative factor in the anemia. In four of the cases, circulating erythrocytes were tagged with radioactive chromium and intestinal blood loss measured by comparing stool and blood radioactivity. Average intestinal blood loss in these four cases shortly after admission was 92·0, 99·3, 57·1, and 251·5 cc. per day, respectively. There was a decrease in relative fecal radioactivity as the blood hemoglobin rose after iron therapy or transfusions. Possible explanations for this phenomenon are offered. In a fifth case (Case 1) no radiochromium studies were performed, but the rise in blood hemoglobin followed shortly after deworming, although the anemia had not responded previously to transfusions or ferrous sulfate therapy.

"It may be speculated that the anemia associated with hookworm infection unfolds somewhat as follows: iron and other components of the blood are sucked by the hookworm and lost by the patient at a certain rate every day. At first the patient is able to replace this from the food he ingests. When the loss exceeds the daily absorption, or possibly if certain mechanisms of blood regeneration fail, blood hemoglobin diminishes, until a new level is reached at which iron loss becomes less because of the lower iron content of the blood. This stable condition may remain for years, or the worm load may increase, or the food diminish, or the mechanisms of blood formation may become inadequate to meet the demands, and from level to level hemoglobin decreases. This goes on until a point at which the hookworm possibly augments its blood consumption, in order perhaps to compensate for the low content of the blood in certain elements. At this time, we might call the disease itself "decompensated" because a vicious circle has been entered in which no new dynamic level of equilibrium can be attained. In such a state are the cases which come into the hospital moribund and in whom transfusions are life saving, both because they replace lost blood, and because they partially inhibit the avidity of the hookworm."

ROCHE, M., PÉREZ-GIMÉNEZ, María E., LAYRISSE, M. & DIPRISCO, Estela. Estudio de la excreción urinaria y fecal del cromo radioactivo Cr^{51} en humanos y su uso como medida de las hemorragias intestinales asociadas con la infección con anquilostoma. [**Study of Urinary and Faecal Excretion of Radioactive Chromium ^{51}Cr in Man, its Use in the Measurement of Intestinal Blood Loss associated with Hookworm Infection**] *Archivos Venezolanos de Nutrición.* 1957, Dec., v. 8, Nos. 1/2, 5–31. [19 refs.] English summary.

See also this *Bulletin*, 1957, v. 54, 1336.

ROCHE, M., PÉREZ-GIMÉNEZ, M. E. & LEVY, A. Un método de trazadores radioactivos para medir la pérdida y reabsorción de hierro en lesiones hemorrágicas gastrointestinales. [**A Method for Estimating Blood Loss and Reabsorption in Gastro-Intestinal Haemorrhagic Lesions by Means of Radioactive Tracers**] *Archivos Venezolanos de Nutrición.* 1957, Dec., v. 8, Nos. 1/2, 33–8. [Published in English in *Nature.* 1957, Dec. 7, v. 180, 1278–9.]

The English summary appended to the paper is as follows:—

"A new method to determine the reabsorption of iron from gastro-intestinal bleeding lesions is presented. It is based in the subsequent labeling of the blood erythrocytes with Fe-59 and Cr-51 and the comparison of the fecal loss of both elements. In 4 cases infested with various numbers of hookworms the observed reabsorption rate was 37–76%."

ROCHE, M. & PÉREZ-GIMÉNEZ, María E., with the technical assistance of A. LEVY. **Intestinal Loss and Reabsorption of Iron in Hookworm Infection.** *J. Lab. & Clin. Med.* 1959, July, v. 54, No. 1, 49–52, 1 fig. [12 refs.]

This study was made to determine whether the iron of the blood removed by hookworms was totally lost in the faeces, or partly re-absorbed. In 14 patients infested with *Necator americanus,* circulating red cells were tagged with both ^{51}Cr and ^{59}Fe. As the former, which can only enter the intestine in shed blood, is known to be absorbed only in very small amounts, its presence in the faeces is a measure of the primary blood loss. Radioactivity from ^{59}Fe indicates the actual amount of iron lost in the faeces. The difference represents the amount of iron re-absorbed.

The patients were all iron-deficient (plasma iron 15–82 μgm./100 ml., Hb 3·2–14·0 gm./100 ml.); their excretion of ova varied from 0·58 to 11·39 millions per day; the worms recovered from their intestines numbered 102 to 3,861. The intestinal iron loss per day varied from 2·74 to 21·34 mgm., and the proportion of iron re-absorbed from 13·1 to 76·4% of that originally lost. The table giving these facts reveals no definite association between them. For example the iron re-absorbed was not related to the amount lost or to the state of the iron reserves; nor was the primary iron loss dependent in any but the most general manner on the egg count or on the number of worms recovered. *Alan B. Raper*

CHARMOT, G. & REYNAUD, R. Relations entre l'ankylostomose et la drépanocytose. [**Relations between Hookworm Disease and Sickling**] *Bull. Soc. Path. Exot.* 1959, Jan.–Feb., v. 52, No. 1, 29–31.

The following is a translation of the authors' summary:—

In 50 children with the sickling trait hookworms were found in 64%, which corresponds with the infection rate in children in the Brazzaville region. But only 26% of 46 children with sickle-cell disease harboured these parasites. The exclusive existence of haemoglobin S seems therefore to condition a partial resistance to hookworm infection.

[See also this *Bulletin*, 1947, v. 44, 1091; 1956, v. 53, 1044; 1958, v. 55, 424, 1271.] *H. J. O'D. Burke-Gaffney*

BAYLET, R. J. & PAILLET, R. J. Abcès musculaire par *Oesophagostomum* (Dakar). [**Muscle Abscess caused by** *Oesophagostomum*] *Bull. Soc. Path. Exot.* 1959, Jan.–Feb., v. 52, No. 1, 32–4.

HURMUSIADIS, A. [**An Autochthonous Case of** *Strongyloides stercoralis* **Infection in Man**] *Acta Microbiologica Hellenica.* Athens. 1959, May–June, v. 4, No. 3, 96–8. [In Greek.]

RIVAS-GOMEZ, A. La strongyloidiasis en nuestro medio. [**Study of** *Strongyloides* **Infection in Caracas, Venezuela**] *G.E.N.* Caracas. 1958, July–Dec., v. 13, Nos. 1/2, 5–38, 31 figs. [80 refs.]

A review of the literature and a detailed study of 36 cases, of which 4 were fatal.

CHEONG CHEE HOCK. *Ascaris* **in the Right Lacrimal Duct of a Child.** *Proc. Alumni Ass., Malaya.* 1959, June, v. 12, No. 2, 109–10, 1 fig.

See this *Bulletin*, 1956, v. 53, 1456.

LIEN, Shih-Hai. **Radiographic Diagnosis of Biliary Ascariasis.** *Chinese Med. J.* Peking. 1959, June, v. 78, No. 6, 545–55, 5 figs. on pl.

In many parts of China ascariasis is widespread while in Szechuan and Yunnan the incidence is said to be 96–98% of the whole population. It is not surprising that symptoms due to the entry of a worm into the common bile duct are not uncommon. The radiological diagnosis of this condition is therefore of importance, all the more so since this can be followed by manipulation under radiological control which often succeeds in squeezing the worm back into the duodenum.

The diagnostic procedure, which cannot however visualize the worm which has completed its entry into the bile duct, depends upon the demonstration of the radiotranslucent worm outlined by a thin suspension of barium introduced *via* a metal-tipped duodenal tube under direct fluoroscopic observation. When an *Ascaris* has begun to enter the common bile duct its protruding portion can be seen outlined with barium and, though the tail may be made to wave up and down the duodenum by pressure, the point on its body which is gripped at the sphincter of Oddi will remain immobile. The entry of the worm in its entirety into the bile duct will often evoke extreme spasm of the duodenum and the demonstration of this will furnish support to a clinical diagnosis of biliary ascariasis.

When the worm is seen only to be partially immured in the duct, gentle, sustained pressure and massage over the gall-bladder and bile duct may squeeze

it back into the lumen of the duodenum. Even if this is not achieved, however, a worm subjected to such indignity may withdraw spontaneously within the next few hours.

Using the technique outlined above, the author has demonstrated the worm in 40 out of 41 patients suffering from biliary ascariasis, his one failure being in a patient who was shown at subsequent laparotomy to have 2 *Ascaris* completely within the common bile duct.

Short notes are given on all 41 cases, together with full details of 4 illustrative cases and 5 radiographic pictures.

[This is a clear exposition of an art unknown to Western radiologists.]

J. H. Walters

T'UNG, Shang-T'ai & CHOU, Teh-Yi. **Acupuncture combined with Traditional Drug Wu Mei T'ang in Treatment of Biliary Ascariasis. Preliminary Analysis of 48 Cases.** *Chinese Med. J.* Peking. 1959, June, v. 78, No. 6, 542–4.

The authors claim to have treated successfully 48 patients suffering from biliary ascariasis by the employment of acupuncture and a draught containing a decoction of traditional herbs. The acupuncture, in which points, each carrying an individual name, were chosen and a needle was inserted to " the required depth at the appropriate points ", was carried out once or twice daily for not more than 5 insertions, the instrument being retained *in situ* for 20–30 minutes on each occasion.

The anthelmintic decoction of 9 herbs, one of which is given by its Chinese name only, is fully described but is required to be administered in large doses of 200 ml. 4 times daily for 10 doses. The pharmacological action of this preparation is not fully understood. Acupuncture appears to exert effective, if drastic, counter-irritation which alleviates temporarily the severe biliary and duodenal colic which results from the intrusion of the worm into the bile duct.

[This article gives a fascinating vignette of traditional Chinese medicine.]

J. H. Walters

FRAGA DE AZEVEDO, J., GÂNDARA, A. F. & FERREIRA, A. P. Ensaio terapêutico do fermento da *Carica papaia* na ascaridiose. [**Therapeutic Test of the Enzyme of** *C. papaya* **(Papain) in Ascariasis**] *Anais Inst. Med. Trop.* Lisbon. 1958, Mar., v. 15, No. 1, 251–7. [10 refs.]

The English summary appended to the paper is as follows:—

" A therapeutic test was carried out with a product based on the *Carica papaia* ferment, using a scheme of three doses of 2·25 g. which were given on the same day, without preparation, diet or laxative, verifying that the vermifuge is not toxic but only slightly irritant causing slight abdominal pains in 10% of the patients, without irregular migrations of the *Ascaris*.

" The product was effective in 65·2% of simple infections and in 27·7% of infections in which the *A. lumbricoides* was associated with the Ancylostomatidae, verifying an important difference in the action of the product on the *Ascaris* according to whether these are or are not associated with these helminths."

SOUTH PACIFIC COMMISSION. Noumea, New Caledonia. **Filariasis in Netherlands New Guinea** [IYENGAR, M. O. T.]. *Technical Information Circular No. 34.* 1959, July, 8 mimeographed pp.

The form of endemic filariasis in Netherlands New Guinea is nocturnal periodic *Wuchereria bancrofti* infection, restricted to flat, low-lying areas below 1,500 ft. altitude. Until recently it was thought that the vectors were anophelines only, principally of the *Anopheles punctulatus* group of which *A. farauti* was considered to be the most important. Recent researches have shown that in certain areas there are important culicine vectors. The list of known vectors now is *A. farauti*, *A. koliensis*, *A. punctulatus*, *A. bancrofti*, *Mansonia uniformis*, *Aëdes kochi*, *Culex bitaeniorhynchus* and *C. annulirostris*. Endemic areas fall under two heads, presenting marked differences in epidemiology: (a) areas where transmission is solely or mainly by anophelines, and (b) areas where transmission is mainly by culicines.

Where anophelines are vectors, filariasis co-exists with endemic malaria, though the endemic area of filariasis does not cover all that of malaria. For filariasis to become endemic it requires conditions of intense transmission, *i.e.* a high density of anopheline vectors. Anopheles-borne filariasis shows a very low incidence of elephantiasis, rarely higher than 1%, though filarial manifestations such as lymphangitis and hydrocele may not be so uncommon. In areas where culicines are vectors, the elephantiasis rate is 2–6% and the other complications are common. The contrast is due to the greater degree of superinfection in culicine transmission. Anophelines seldom breed so intensely as culicines, and their breeding sites do not ordinarily occur in the immediate vicinity of habitations. Organic pollution of casual water in or near a village reduces anopheline breeding, but positively encourages that of culicines: the latter therefore breed more intensively and closer to the human population, and transmission is thereby favoured.

It was expected that anopheline control undertaken for anti-malaria purposes would interrupt anopheline transmission of filariasis, and experiment has shown that this has indeed happened. A different approach is needed in areas where filarial infection is transmitted solely or mainly by culicines. Most such areas do not come within the scope of the malaria control scheme, and anyway residual spraying is not effective against culicines. The main epidemiological point to be considered is that intense transmission, producing a high percentage of elephantiasis, etc., takes place in villages situated in very close proximity to swamps. Thus heavy pollution of the swamp water favours intensive culicine breeding, and the vectors have easy access to the population. Prevention of pollution and larvicidal mosquito control are out of the question. Permanent drainage might be possible of small swamps only. The only truly permanent control measures would be the grouping together of the populations of several small villages on selected sites at least half a mile from the breeding grounds of the culicine vectors, thus reducing water pollution and vector-human proximity simultaneously. In known areas where such conditions prevail naturally, the incidence of filariasis, and specially of its complications, is known to be low. The objection to this measure is that the people prefer to live close to the swamps in which sago, their staple diet, grows: the scheme should therefore be combined with the attractions of agricultural, educational, medical and other development. The other alternative is mass prophylaxis

with diethylcarbamazine monthly for at least 5 years. The inclusion of a filariasis section in the country's division of malariology is suggested.

[As this interesting document is not readily available in the original, it has been given a fairly full abstract.] *B. B. Waddy*

De Rook, H. & Van Dijk, W. J. O. M. **Changing Concept of** *Wuchereria bancrofti* **Transmission in Netherlands New-Guinea.** *Trop. & Geograph. Med.* Amsterdam. 1959, Mar., v. 11, No. 1, 57–60. [12 refs.]

In Dutch New Guinea *Wuchereria bancrofti*, showing a nocturnal periodicity, is the causative organism of human filariasis, *W. malayi* being confined to imported carriers. In some parts of New Guinea the incidence of malaria and filariasis are closely related and *Anopheles* mosquitoes belonging to the *punctulatus* group have been shown to be the principal vectors. Some areas, however, such as the Berau and Bamgi-Ia regions, have a high incidence of filariasis associated with an absence of endemic malaria [this *Bulletin*, 1957, v. 54, 1214; 1958, v. 55, 1260].

Full-grown infective larvae of *W. bancrofti* have now been found in natural infections of 5 species of culicine mosquito—*Culex fatigans*, *C. bitaeniorhynchus*, *C. annulirostris*, *Aëdes kochi* and *Mansonioides uniformis*—and these, and 2 other species—*Culex squamosus* and *Mansonioides papuensis*—have been infected experimentally. The 5 species found with natural infections all enter houses to feed on man and breed in close proximity to man. The 2 most important species of culicine are believed to be *Mansonioides uniformis* and *Culex annulirostris*, while *C. fatigans*, which has only recently been imported into the country, is an increasingly dangerous vector. *B. R. Laurence*

Mello, A. L., Ferraz, D. M. & Rachou, R. G. Resultado de inquéritos hemoscópicos para filariose humana realizados no Rio Grande do Sul no triênio 1954–1956. [**Blood Surveys for Filariasis in Rio Grande do Sul, Brazil, in 1954–1956**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1958, Apr., v. 10, No. 2, 211–12.

The English summary appended to the paper is as follows:—

"From 1954 to 1956 the authors made hemoscopic surveys for bancroftiasis in 24 localities of 12 counties (= 'municípios') of the State of Rio Grande do Sul examining 39,754 persons. Carriers of microfilariae of *bancrofti* were found only in Pôrto Alegre."

Ferraz, D. M., Mello, A. L. & Rachou, R. G. Comprovação da transmissão da filariose bancroftiana em Pôrto Alegre (Rio Grande do Sul). [**Transmission of** *Wuchereria bancrofti* **in Pôrto Alegre, Rio Grande do Sul**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1958, July, v. 10, No. 3, 275–6.

The English summary appended to the paper is as follows:—

"The transmission of bancroftiasis in Pôrto Alegre (Rio Grande do Sul)

has been proved; among 2,342 dissected specimens of *Culex pipiens fatigans* caught indoors, the authors found one with infective larva of *W. bancrofti*."

RACHOU, R. G., PIRES, W. M. & MOURA LIMA, M. Filariose bancroftiana em São Luiz, Maranhão: resultado de inquérito feito em 1957. [**Bancroftian Filariasis in Sao Luiz, Maranhao, Brazil**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1958, Jan., v. 10, No. 1, 61–4.

The English summary appended to the paper is as follows:—

"A new focus of bancroftiasis has been found in Brazil: São Luiz, Capital of the State of Maranhão. Percentage of microfilariae carriers, among 8,776 examined persons: 0·6%. *Culex pipiens fatigans* is the vector: 8·2% infected with larvae of all stages and 0·6% with infective larvae (the entomological survey has been done only in houses with microfilariae carriers and in 5–6 houses next to each one of them)."

GILLES, H. M. & WILLIAMS, K. **Effect of Heparin** *in vivo* **on the Release of Microfilariae of** *Wuchereria bancrofti* **into the Peripheral Blood.** [Miscellanea.] *Ann. Trop. Med. & Parasit.* 1958, Dec., v. 52, No. 4, 516–17.

YOELI [this *Bulletin*, 1957, v. 54, 986] claims that a partial release of the microfilariae of *W. bancrofti* followed intravenous heparin injections given during the day. Gilles and Williams followed the periodicity of 14 *W. bancrofti* carriers, 4 of whom were heavily infected, at 10 a.m., 11 a.m., noon, 2 p.m., 4 p.m. and 10 p.m. for 2 days, and 125 mgm. of heparin given at 9.55 a.m. produced no significant differences on the third day. *W. E. Kershaw*

WHARTON, R. H. **A Simple Method of Mounting and Preserving Filarial Larvae.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 4, 729–30.

The author, from Kuala Lumpur, uses a formol-glycerol method for preparing semi-permanent mounts of filarial larvae as a result of a suggestion by Captain D. PRICE of the U.S. Army Medical Corps; more recently he has found it satisfactory also for preparation of mosquitoes for subsequent dissection. It is probably less satisfactory for finding immature larvae than the Mayer's acid haemalum method described by NELSON [this *Bulletin*, 1958, v. 55, 1360] but involves less handling of mosquitoes, and mature larvae, which remain in good condition, are readily identified.

The medium consists of 10 parts formaldehyde solution, 5 parts glycerol and 85 parts distilled water: 0·0003 part methylene blue may be added.

For preparing semi-permanent mounts of larvae from freshly killed mosquitoes dissected in normal saline, the larvae are killed by the addition to the saline of a drop of fresh Bles fluid (70% alcohol, 90 parts; formaldehyde, 7 parts; glacial acetic acid, 3 parts): or the larvae may be transferred to a clean drop of saline to which the Bles fluid is added. After 2 to 3 minutes the larvae are transferred with a fine needle to a drop of the mounting medium, on

the centre of a cell of about $\frac{5}{8}$ (16 mm.) inch diameter on another slide. A 16 mm. cover-slip is placed on the drop of formalin-glycerol which should fill the cell. Excess medium is withdrawn with filter paper and the preparation sealed with several layers of quick-drying paint. Larvae thus mounted have been found to be in good condition after more than 3 years: the mounts should keep indefinitely if they are properly sealed. Mature larvae are easier to handle than immature; sausage-stage larvae are especially easily damaged and tend to stick to a needle that is not completely clean.

For preserving mosquitoes for dissection they are killed in Bles fluid (or hot 70% alcohol) and transferred to formalin-glycerol medium without methylene blue; afterwards they are dissected in the medium with methylene blue. The larvae are easily found as they take the stain more rapidly than the muscles of the mosquitoes. The muscles are very firm and require thorough teasing before immature larvae can be found. Mature larvae are found much more rapidly, but care is required to avoid breaking them, especially if they are in the proboscis or head.

The characteristics of the larvae are preserved clearly and they may be identified as easily as in fresh preparations. In the case of *Wuchereria* infection in mosquitoes the position and appearance of the larvae in the muscles are seen clearly in preserved specimens. The firmness of the muscles allows the exoskeleton to be dissected away and the longitudinal or vertical position of the larvae in the muscles to be determined with accuracy.

A similar mounting method can be used for preparations of malaria oöcyst and sporozoite preparations, but the saline should be flooded with formol-glycerol and not with Bles fluid. The infected stomach or gland is transferred to the ringed slide and much of the appearance of a freshly dissected specimen is retained by the resulting preparation. *H. J. O'D. Burke-Gaffney*

RACHOU, R. G. & SCAFF, L. M. Redução da microfilaremia de *Wuchereria bancrofti* com Hetrazan em esquemas de tratamento de duração variável. [**Reduction of Microfilaraemia due to** *Wuchereria bancrofti* **with Diethylcarbamazine in Treatment Schedules of Varying Duration**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1958, July, v. 10, No. 3, 303–26, 7 graphs. English summary.

This paper extends previous studies by the authors on the use of diethylcarbamazine in the treatment of carriers of *Wuchereria bancrofti* in Belém, Brazil [this *Bulletin,* 1956, v. 53, 638, 639].

After a general survey of the subject and of previous results they describe the results obtained with 4 "long courses" and 3 "short courses" of diethylcarbamazine. The long courses consisted of 6 mgm./kgm. daily for 7, 10, 15 or 21 days and the short courses of 6 mgm./kgm. daily for 1 or for 3 days or 12 mgm./kgm. for 1 day only.

Monthly blood examinations and microfilaria counts were made for 18 months after treatment in those who had the long course, and 3-month examinations were made for 1 year in those who had the short course. The object was to evaluate reduction of microfilarial density in relation to the daily doses and their duration.

The results are set out in great detail in 7 graphs and 11 tables.

With the long courses density of microfilariae was greatly reduced and the reduction was maintained throughout the 18 months: 27% to 35% of the carriers were completely negative for microfilariae during that period. No significant differences were recorded between the 4 schedules, although there was some correlation between the duration of treatment and the reduction in microfilariae.

Similar, though less sharp, results were found with the short courses.

The authors as a result of these studies recommend the use of a single dose of 6 mgm./kgm. every 6 or 12 months as a prophylactic measure for the whole population, whether they are infected or not. It is simple and economic and the cost of the large quantity of diethylcarbamazine required would be offset by the greatly reduced routine haematological work required for the discovery of carriers, mainly in areas where nocturnal periodicity of the microfilariae requires work to be done at night.

They add that a field trial on these lines is already in operation in one area in southern Brazil. *H. J. O'D. Burke-Gaffney*

NAIR, C. P. & ROY, R. **Filariasis in Kerala State. Part IV. Filaria Survey of Eriyad Panchayat, Cranganore Taluk.** *Indian J. Malariology.* 1958, Sept., v. 12, No. 3, 195–201, 1 map.

Eriyad Panchayat is in the Trichur district, Kerala State, S.W. India. It is bounded on the north by Edavilanga village, on the south by the Periyar River and on the west by the Arabian Sea. The soil is sandy and the subsoil water level high. There are extensive coconut groves; the main occupations are fishing and the coir industry.

The key to the present question lies in the fact that almost every house has a compound with one or more ponds abounding with an overgrowth of *Pistia stratiotes*. These ponds are used for washing and bathing and also for watering the coconut trees and for soaking their husks.

There are 2 villages, Azhikode and Eriyad. The total population of the Panchayat (1951 census) is 19,011 made up of 9,307 males and 9,704 females.

A parasitological and clinical survey was made in December 1957. Thick blood films of 20 cmm. were made from 8.30 p.m. to 3 a.m. After dehaemoglobinization the films were stained with JSB (Jaswant-Singh and Bhattacharji) stain for 5 minutes. The parasite in every case was *W. malayi*. The survey included 1,787 persons, or 9·4% of the total population. The infection rate of males was slightly higher than that of females and it followed the well-accepted rule of more or less progressive increase up to the age of 20, after which it remained static.

The youngest person infected was an infant 10 months old with 9 microfilariae per 20 cmm. of blood. The filarial disease rate for the whole community was 11·2% and it rose progressively with age. 201 persons had manifestations of filarial disease and of these 10% were positive for microfilariae.

From a dissection of 292 female mosquitoes, developmental stages of the parasite were found in 2 *Mansonioides annulifera* and in 1 *M. uniformis* only. These mosquitoes were breeding in ponds overgrown with *Pistia stratiotes*.

[This study can be regarded as a pilot survey, based on less than 10% of the total population.] *Philip Manson-Bahr*

EDESON, J. F. B. & BUCKLEY, J. J. C. **Studies on Filariasis in Malaya: On the Migration and Rate of Growth of *Wuchereria malayi* in Experimentally Infected Cats.** *Ann. Trop. Med. & Parasit.* 1959, Apr., v. 53, No. 1, 113–19, 2 text figs. & 4 figs. on pl.

EDESON and WHARTON [see this *Bulletin*, 1958, v. 55, 196] have transmitted *W. malayi* from man to the domestic cat and have studied the migration and growth rate of the infective larva of this parasite in this animal.

The migration of the infective larvae is rapid but the rate of the later migration is influenced by the site of inoculation of infective larvae. Whether the adult worms travel along the lymphatic vessels or in the tissue is not clear. *W. malayi* will develop almost anywhere in the lymphatic system and that the inguinal, popliteal and sacral glands are most commonly involved is probably due to the infective larvae being inoculated usually in the groin. That so many larvae settle in the popliteal gland may be related to the fact that elephantiasis due to *W. malayi* is almost always in the legs, rarely extending above the knee.

The common pattern of development in many nematodes, in having two moults in the definitive host, is followed by *W. malayi* and by *Litomosoides carinii* [see *ibid.*, 1952, v. 49, 789] (in which the moults appear at about 10–15 days, and 23–24 days). In *W. malayi* moulting occurs at 9–10 days, and at about 35–40 days.

The adults of *L. carinii* complete their growth in 2½ months and SCOTT [see *ibid.*, 1947, v. 44, 447] correlated this rapid growth and sexual maturity within 50 days, with the short life-span of the cotton rat. This now seems doubtful since *W. malayi* attained sexual maturity within 75 days, though females continue to grow up to 10 months. *W. E. Kershaw*

LAMY, L. & GIRARD, G. G. Observation d'un cas de filariose oculaire en France. [**A Case of Ocular Filariasis in France**] *Bull. Soc. Path. Exot.* 1959, Jan.–Feb., v. 52, No. 1, 28–9.

They call it *Dirofilaria conjunctivae* but say that it is probably identical with *D. repens* in a non-specific host.

LAGANA, I. [**On Two Cases of Filariasis *Loa loa* on Greek Patients coming from Belgian Congo**] *Acta Microbiologica Hellenica.* Athens. 1959, May–June, v. 4, No. 3, 77–80. [In Greek.] English summary (9 lines).

KIRK, R., MORGAN, H. V., HASEEB, M. A. & SATTI, M. H. **Onchocerciasis in the Sudan Republic.** *Ann. Trop. Med. & Parasit.* 1959, Apr., v. 53, No. 1, 97–102. [37 refs.]

The object of this paper is to give an up-to-date summary of the information available on onchocerciasis in the Sudan, much of which has appeared previously only in unpublished reports. The geographical distribution has not yet been completely mapped. The Bahr el Ghazal area was the first discovered, but the disease also occurs patchily along the Abyssinian border, over a greater area than that discovered by BLOSS [this *Bulletin*, 1950, v. 47, 146], and a new

focus in the north was discovered recently [MORGAN, *ibid.*, 1958, v. 55, 1147]. As far as is known, *Simulium damnosum* is the only vector in the Sudan, *S. neavei* not having been found by LEWIS [*ibid.*, 1953, v. 50, 543, and 1954, v. 51, 743]. Clinically, patients most commonly come for treatment of eye lesions, genital elephantiasis or craw-craw. Numerous cases of epilepsy have been discovered in association with onchocerciasis, but it is difficult to be certain that this is more than coincidental. Chemotherapy with diethylcarbamazine or suramin has been used; suramin has given spectacular improvement of vision in anterior segment blindness, but also has given dangerous and fatal reactions. Lewis [*loc. cit.*] has expressed pessimism about the prospect of entomological control in the Sudan. "The present writers are unwilling to accept these pessimistic conclusions . . . even partial control may be of value in preventing blindness by reducing the intensity of infection . . . and it may be possible to attack the individuals which survive the adverse conditions of the dry season and so prevent their initiating multiplication at the beginning of the next season." [The abstracter, while respecting the authority of Lewis's work, would point out that so far almost every scheme for the control of *Simulium* has had far greater success than was expected, and echoes the authors' call to action.] *B. B. Waddy*

COMITÉ DE L'ENTENTE FRANÇAISE. L'Onchocercose. Fléau social en Afrique. Première opération prophylactique d'envergure en Afrique Equatoriale Française. [**Onchocerciasis, a Social Scourge in Africa. First Widespread Prophylactic Operation in French Equatorial Africa**] 40 pp., 8 figs. & 1 map on 9 pls. [? 1957.] Paris VIIe: 11 bis, Impasse de la Visitation.

This booklet gives a comprehensive semi-popular account of the campaign against onchocerciasis in the Mayo Kebbi area of French Equatorial Africa. It is made clear that this potentially fertile area was rapidly becoming depopulated through the ravages of onchocerciasis, and the campaign was a matter of urgent necessity. An account of the anti-vector aspects has already been published [TAUFFLIEB, this *Bulletin*, 1957, v. 54, 733] but some apparently unpublished clinical information is given. Out of 16,116 persons examined 1,819 (11·28%) had ocular lesions. 507 had choroido-retinal lesions and 315 [many possibly the same persons] optic nerve lesions. Partial or complete lens opacities were extremely frequent, and their early incidence was specially marked in females between 26 and 45 years. The anterior segment lesions presented no special features. Treatment was given with Notézine [diethylcarbamazine] to destroy the microfilarial reservoir, and curative treatment with Moranyl [suramin] was given also to those with organic complications. The maximum dose of Moranyl was 5 intravenous injections of 1 gm. There were 16 deaths out of 3,676 treated, but 7 of these were in old people. Nodulectomy was practised by an itinerant surgical team. 1·7% of nodules were found on the head.

Details of insecticide preparations used have been rendered out of date by more recent French research, *e.g.*, D'AUBENTON and BLANC [*ibid.*, 1959, v. 56, 961].

[The booklet is very readable and well illustrated and deserves a place on the bookshelf of anyone interested in the practical aspects of the onchocerciasis problem.] *B. B. Waddy*

ROJAS, C. Infección parasitaria apendicular por *Enterobius vermicularis*. [**Caecal Infection by** *Enterobius vermicularis*] *Bol. Chileno de Parasit.* 1959, Apr.–June, v. 14, No. 2, 26–8. [17 refs.]

The English summary appended to the paper is as follows: —

"The presence of *Enterobius vermicularis* in the appendicular lumen was analyzed in material provided by 1020 appendectomies performed at the Surgical Ward of the hospital at Traiguén between 1954 and 1957. A total of 119 positive cases was found among 914 adults (595 women and 319 men) and 106 children under age 14."

ATIAS, A. & RAMIREZ, M. Oxyuriasis: Ensayo terapéutico con hexahidrato de piperazina en cuatro días de tratamiento. [**Oxyuriasis: an Assay of 4-Day Treatment with Piperazine Hexahydrate**] *Bol. Chileno de Parasit.* 1959, Apr.–June, v. 14, No. 2, 28–9.

The English summary appended to the paper is as follows: —

"Effectiveness of piperazine hexahydrate against oxyuriasis was tested in short-term treatments (4 consecutive days) applied to 38 patients; simultaneously, the patients were thoroughly instructed about sanitary measures. Control of treatment by means of the Graham test revealed 60·5% cures and 39·4% failures. Although the small number of patients tested does not yield statistical conclusions, the authors recommend to keep up the treatment for a period longer than four days."

WARDA, L. Działanie niektórych preparatów piperazynowych na jelitowe postacie włośni (*Trichinella spiralis*). [**The Effect of some Piperazine Preparations upon Intestinal** *Trichinella spiralis*] *Wiadomości Parazytologiczne*. Warsaw. 1959, v. 5, Nos. 2/3, 299–306.

The English summary appended to the paper is as follows: —

"Attempts were made at the treatment of experimental trichinellosis in mice (253 animals) by means of piperazine preparations. The experiments with animals were preceded by investigations *in vitro*. Hydrate of piperazine showed the strongest effect *in vitro*. There was observed that males are more sensitive to piperazine compounds than females.

"The experiments with mice show that piperazine compounds administered during 6 days, beginning from the 2nd or 8th day after infection, have a strong effect upon adult males (81–97% of reduction), and a much weaker on females. The highest decrease in the number of females was obtained with hydrate of piperazine preceded by administration of magnesium oxide (56% of deduction).

"The strongest influence of piperazine preparations on trichinella larvae (58·1% of reduction) through the effect on adult parasites during the intestinal period, was attained in a series of mice treated with hydrate of piperazine, beginning on the 8th–13th [day] after infection, this treatment being preceded by introduction of MgO by means of a probe. A relatively high decrease in the number of larvae in the diaphragm is also caused by introducing hydrate of piperazine (a single dosage) directly into the small intestine.

"Considering the lack of any causal treatment of trichinellosis, even in cases

of early diagnosis, a trial with hydrate of piperazine is suggested by introducing this preparation intraduodenally, or with this hydrate preceded by magnesium oxide introduced into the stomach—for clinical examination."

DEFICIENCY DISEASES

BASSIR, O. **Nutritional Studies on Breast Milk of Nigerian Women; Supplementing the Maternal Diet with a Protein-Rich Plant Product.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1959, May, v. 53, No. 3, 256–61, 2 figs. [16 refs.]

" 1) Sixteen Nigerian mothers in the first 6 months of lactation were selected at random and used in a feeding experiment lasting 3 months, with a view to assessing the value of supplementing their home diets with 30 g. of soya flour daily.

" 2) The women were paired according to their stage of lactation and socio-economic class. One group received the soya in addition to their ordinary food.

" 3) An increase in the output of breast milk was obtained, after 4 weeks, in the women feeding on the soya flour. This increase was more marked after 8 weeks.

" 4) The composition of the milk was not significantly altered during the course of the experiment. The constituents estimated were total nitrogen, non-protein nitrogen, ' cream ', calcium, phosphorus, and phosphatase."

[See also this *Bulletin*, 1956, v. 53, 1373.]

GONGORA, J. & MCFIE, J. **Malnutrition, Malaria and Mortality. The Use of a Simple Questionnaire in an Epidemiological Study.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1959, May, v. 53, No. 3, 238–47, 1 map.

The original intention of the special study with the Individual Record Questionnaire was to give a reliable estimate with which to compare routine reports. The form, eventually distributed and explained to medical assistants in charge of 76 dispensaries in Uganda, asked for information on all children seen under 6 years of age, with name, age, sex, diagnosis, the number of sibs dead or alive, with ticked comment on the presence of emaciation, thin and pale hair, anaemia, thin and loose skin, palpable spleen, oedema, and the examiner's conclusion whether the child suffered from malnutrition.

Analysis of 22,036 records from 72 dispensaries in which the authors had participated in the examinations, showed that children aged under 1 year were in proportionate excess, that malnutrition was suspected in 6% to 22% of children in different districts, and these figures are very considerably higher than had previously been reported.

Analysis of the value of the figures shows that some reliability has been achieved in response to the finally adopted form and system of explanation; the proportions of sibs which were alive or dead may be used for making

comparisons between districts, and the actual percentage dead varied from 17·2% to 31·5%. The partial correlation coefficient of this sib mortality with the spleen rate, holding malnutrition constant, is 0·54, and conversely with malnutrition holding the spleen rate constant, is 0·22. There is therefore a close association between evidence of intensity of malaria and mortality, and less association between malnutrition and mortality. *G. Macdonald*

Rao, B. R. H., Rao, P. S. S. & Klontz, C. E. **General Health and Nutrition Survey of the Rural Population in Pennathur. Part IV: Protein Nutrition.** *Indian J. Med. Sci.* 1959, May, v. 13, No. 5, 401–9. [42 refs.] **Part V: Vitamin Nutrition.** *Ibid.*, 410–19. [32 refs.]

These two papers are a continuation of the report of an important diet survey in South India; the first papers have already been abstracted [this *Bulletin*, 1959, v. 56, 964].

The mean intake of protein was 48 gm./day/consumption unit. This figure is based on the records obtained from 40 families containing 154 adults and 112 children. In 7 families the intake was very low, less than 35 gm. The percentage of animal protein was low, averaging only 5% of the total. Serum protein levels were determined in 436 adults and the mean level for total proteins was 7·1 gm./100 ml. and for serum albumin 4·2 gm./100 ml. Of these adults, 40 or approximately 10% had serum albumin levels below 3·5, which would certainly be considered below the physiological range. The number of people with low albumin levels was less than might be expected from the low intake of dietary protein. Of 681 persons clinically examined 2·3% had minimal oedema of the legs and only one case of marked oedema was seen.

The first paper concludes with a good discussion of ways and means of increasing dietary protein and emphasizes the importance of the possibilities of using relatively cheap vegetable sources. The need for education is stressed and the desirability of variety in the choice of foods.

The second paper deals mainly with vitamin A, riboflavin and vitamin C, there being no obvious evidence of deficiency of other vitamins.

The mean dietary intake of vitamin A activity in the 40 families was 866 IU/day/consumption unit, which is far below acceptable standards. Most of this was from vegetable sources. The mean serum levels of vitamin A were 52 and 47 IU/100 ml. for males and females respectively, which is less than one-half the usual level found in Europe and North America. Over 40% of the sera examined had very low levels, below 40 IU/100 ml. Clinical evidence of vitamin A deficiency was widespread (xerosis conjunctiva 17–21%, xerosis cornea 3–8%, dry and rough skin 11–22%, marked follicular changes 3–7%). Over one-third of the children examined showed clinical signs suggestive of vitamin A deficiency.

The mean dietary intake of riboflavin was 0·49 mgm./day/consumption unit, which is only 50% of the lowest estimates of physiological need. Angular stomatitis was commonly seen in the children and a glazed and fissured tongue and corneal vascularity with lachrymation were frequent in adults. These signs are very reasonably taken as evidence of widespread lack of riboflavin.

The mean dietary intake of ascorbic acid was 26 mgm./day/consumption

unit, but this figure takes no account of losses in cooking and washing. Characteristic skin manifestations of scurvy were not observed, but 9% of those examined had bleeding gums, possibly attributed to deficiency of the vitamin. This may also contribute to the widespread anaemia (17% of those examined had haemoglobin values below 10 gm./100 ml.).

The paper ends with a section on prevention, which emphasizes the need for a well sustained education campaign to initiate a programme of home gardening and to encourage the liberal use of green vegetables and cheap locally available fruit. *R. Passmore*

FRAGA DE AZEVEDO, J., GÂNDARA, A. F. & FERREIRA, A. P. Estudos sobre a nutrição na Província de Timor. 1. Apreciação do estado de nutrição. *Anais Inst. Med. Trop.* Lisbon. 1958, Mar., v. 15, No. 1, 135–53, 5 figs. 2. Inquéritos alimentares. [**Nutrition Studies in Timor. I. Enquiry into the Nutritional State. II. Investigation of Food Habits**] *Ibid.*, 155–79, 1 fig. [21 refs.]

The English summaries appended to the paper are as follows: —

i. " An inquiry on the nutritional state in Portuguese Timor was carried out, on 2,927 Melanoasiatics of whom 207 were infants, 242 adults and 2,478 between 3 and 20 years of age.

" Clinical examination on the physical development, state of the gums, lingual, buccal and conjunctival mucosa was made as well as on the lymphatic, dental and abdominal wall state and also on the blood pressure.

" Laboratory examinations on red blood corpuscles, hemoglobin, sedimentation velocity, proteinaemia, proteinogramme, were carried out.

" Other laboratory examinations concerned the hemoglobin and the red blood cells in mixed persons and Europeans between 7 and 14 years of age.

" Results and conclusions are presented."

ii. " Food investigations were carried out in Portuguese Timor of the qualitative (carnet d'achat) type in 29 centres which enabled us to obtain an approximate relative idea of the food habits of the Melanoasiatic population, especially in Dili, where 27 families were studied, and Laclubar, where 171 statements were taken.

" The quantitative aspect was only studied in relation to the values of the official food tables for the native worker and with regard to economical-social category corresponding to assistant nurse and servant, for which a preliminary enquiry was made."

WILLIAMS, R. R., MCGANITY, W. J., COMBS, G. F. & KERTESZ, Z. I. **A Nutrition Survey of the Armed Forces of the Republic of Korea.** *J. Nutrition.* 1959, June, v. 68, Suppl. 1, pp. vi + 80, 9 figs. [Numerous refs.]

BASCOULERGUE, P., DEPOUX, R. & CHARMOT, G. Le kwashiorkor au Moyen-Congo. [**Kwashiorkor in the Middle Congo**] *Bull. Soc. Path. Exot.* 1958, Nov.–Dec., v. 51, No. 6, 1008–16.

Kwashiorkor is rare in the rural districts near Brazzaville, owing to late weaning and a traditional, varied diet. It is not common in the town, but the

clinical records of 9 cases are reported attributable to poverty and unemployment. It is commonly associated with ankylostomiasis. Acetazolamide seems to assist in removing the oedema. *R. Passmore*

RAO, K. S., SWAMINATHAN, M. C., SWARUP, S. & PATWARDHAN, V. N. **Protein Malnutrition in South India.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 4, 603–39, 7 figs. [24 refs.]

This is a record of a very thorough survey carried out in the states of Madras, Mysore, Kerala and Andhra Pradesh. The well-known poor South Indian vegetarian diets are described in which cereals provide the greater proportion of the calories. Although children are breast fed for a long time, lactation is usually inadequate after 6 months to supply the full needs of the child. Marked retardation of growth is common. Out of 4,536 children examined 1% were found to have kwashiorkor. The disease may be responsible for up to 16% of the children admitted to hospitals, but many children remain at home. Both lack of awareness on the part of the mother and lack of hospital facilities may be responsible. Haemoglobin levels remain well below acceptable standards, although malaria has been effectively controlled in all the areas surveyed.

This report is well presented and gives a clear picture of the poor state of health of many children in South India. *R. Passmore*

DEAN, R. F. A. **Kwashiorkor in Malaya.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 4, 727–9.

Out of 3,145 Malay children aged 1 to 4 years examined, 189 cases of kwashiorkor were found, of whom 123 were in the Perak district, the only district in which the disease was common. The high incidence here may be due to the custom of artificially restricting the diet of women after delivery. Fish is also forbidden to children until they are 2 years old. A fuller investigation of the causes of the disease in this district is desirable. *R. Passmore*

KAHN, E. **Dehydration in Children suffering from Protein Malnutrition (Kwashiorkor).** *South African Med. J.* 1959, June 13, v. 33, No. 24, 501–2.

This paper stresses the fact that dehydration as judged by diminished elasticity of the skin over the chest and abdomen may be associated with nutritional oedema of the lower limbs in protein malnutrition. Diarrhoea is commonly associated with the dehydration. Low levels of serum sodium (less than 124 mEq. per litre) were found in 11 out of 27 dehydrated children and of serum potassium (less than 3·5 mEq. per litre) in half of them. In 40 children with protein malnutrition but with no dehydration, the mean of the serum electrolyte levels was only just below normal standards. Malnourished children with dehydration rarely survive unless they receive intravenous fluid. A solution containing 35 mEq. of sodium and 27 mEq. of potassium per litre is used and about 100 ml./lb. body weight given in the first 24 hours.

R. Passmore

SRIKANTIA, S. G. & GOPALAN, C. **Renal Function in Nutritional Oedema.** *Indian J. Med. Res.* 1959, July, v. 47, No. 4, 467–70.

"1. Renal function in 5 cases of nutritional oedema was investigated by studying the inulin and diodone clearances.

"2. The inulin and diodone clearance values were found to lie within the normal range, thereby indicating normal renal plasma flow and glomerular filtration.

"3. The low urine minute volume in spite of normal clearances would appear to indicate increased tubular reabsorption."

CASTILLO, F., HASBÚN, R. E. & CUEVAS, Celia. Volumen plasmatico y sanguineo y niveles de potasio en el sindrome pluricarencial infantil. [**Plasma and Blood Volumes and Potassium Levels in Kwashiorkor**] *Archivos Colegio Med. El Salvador.* 1957, Dec., v. 10, No. 4, 258–62. [10 refs.]

WALT, F. **Anaemia in Kwashiorkor.** *J. Trop. Pediatrics.* London. 1959, June, v. 5, No. 1, 3–9, 1 fig. [20 refs.]

On the subject of the anaemia of malnutrition in children in tropical and primitive conditions, there is a growing recognition that: (a) the type of anaemia varies from one place to another; (b) specific therapy often fails to cure the anaemia, but may alter its type; (c) it is rarely possible to find any simple explanation for the anaemia; (d) the anaemia is but part of a generalized interference with cellular metabolism which must be corrected before the anaemia can be cured, and that this correction may take many weeks of treatment.

This paper from Durban describes 2 forms of anaemia seen in children with kwashiorkor. (1) Megaloblastic anaemia is estimated to occur in 15–20% of the children. The severe forms develop with great rapidity, are responsive to folic acid, but transfusion is the recommended treatment. When megaloblastosis of the marrow is less severe it is usually not the sole case of the anaemia, since it can be cured by folic acid while the anaemia remains. (2) Normocytic orthochromic anaemia is found in all children with kwashiorkor, including those who have recovered from a megaloblastic phase. A constant pattern appeared in 23 children who had been treated with skimmed milk, antibiotics, folic acid, and vitamins B and C; marked clinical improvement, and a steady restoration of the total serum proteins took place within 28 days, but the Hb% fell during the first week (owing to haemo-concentration), and remained below the initial value. This refractory state could not be attributed to infection in most of the patients.

Further studies in which extra iron is used are now in progress and it is suggested that treatment with many haematinics may ultimately be the therapy of choice.

Alan B. Raper

KAHN, E. & STEIN, H. **Purpura in Kwashiorkor.** *Brit. Med. J.* 1959, July 18, 66–8, 1 fig. [14 refs.]

The occurrence of purpura in the kwashiorkor syndrome is well known, though in Johannesburg, where 600 to 800 such patients are treated annually

in the Baragwanath Hospital, it is seen in only 3–5% of children showing this pattern of severe malnutrition. The authors formed the opinion that purpura in such patients was rarely caused by haematological defects but was associated unusually frequently with a primary infection, either tuberculosis or salmonellosis. They set out to test this hypothesis by careful investigation of a series of 23 children showing kwashiorkor with purpura.

The patients ranged in age from 5 months to 8 years and included 18 males and 5 females. All were severely malnourished. 13 were oedematous, 17 showed an acute dermatosis [? pellagrinoid] and 6 had marked hepatomegaly. The purpuric rash was distributed over the clavicles, lower abdomen and groins, and was often coalescent.

In 2 patients only was it possible to demonstrate a causal haematological defect, in both of whom thrombocytopenia and a prolonged bleeding-time were discovered. In both cases the bone-marrow was hypoplastic with a deficiency of megakaryocytes; this was attributed in the case of one child to the previous administration of chloramphenicol. The coagulation time of all patients was normal, though the prothrombin indices were less than 100% in 21, the lowest level being 54%. A similar depression of prothrombin level was demonstrated however in a consecutive series of 23 kwashiorkor patients who showed no purpura.

Evidence of infection with the tubercle bacillus or with salmonella organisms was found in 16 of the 23 purpuric children, this high incidence (70%) contrasting strikingly with the much lower incidence of infections (8% with salmonellosis and 10% with tuberculosis) noted in non-purpuric kwashiorkor patients in 1956. Of the present series of 16 patients, 8 were proved to be suffering from active pulmonary tuberculosis which was of miliary type in 2, and 8 from salmonella infections, isolations being made from the blood in 4 and from rectal swabs in 4 instances. The organisms recovered were *Salmonella typhi*, *S. typhi-murium*, S. San Diego and S. Adelaide from the blood, S. Kentucky, S. Johannesburg, S. Aberdeen and S. Newport from the colon.

From an examination of the literature the authors conclude that allergy to the tubercle bacillus adequately explains the occurrence of purpura in kwashiorkor precipitated by tuberculosis, while in those patients whose malnutrition is associated with a salmonella infection, purpura is a manifestation of salmonella septicaemia.

[The important point is that the occurrence of purpura in a patient showing the kwashiorkor syndrome calls for a search for infection with the tubercle bacillus or a salmonella organism.] *J. H. Walters*

Velasco C., F. J. Estudio de las lesiones hepaticas y su evolucion en el sindrome pluricarencial. [**Study of Hepatic Lesions and their Development in Kwashiorkor**] *Archivos Colegio Med. El Salvador.* 1957, Dec., v. 10, No. 4, 245–57, 5 figs. [36 refs.]

The author studied 25 children with kwashiorkor from various parts of El Salvador by means of liver biopsy and liver function tests. Subjects were selected on the basis of the classical signs of the disease and precautions were taken, which are described, to ensure that no serious complications would

arise. The clinical features are described briefly and the findings tabulated. The commonest liver lesions found at biopsy were lymphocytic infiltration of the portal and periportal spaces (18 cases), lobular disorganization (16), fatty changes (15) and fibrosis (7). The principal change in the liver function tests was a fall in the total proteins, especially in the albumin fraction.

The number of liver lesions varied from 1 to 4: nearly half of the patients had 3.

In 14 patients biopsies were repeated 28 days after treatment. Improvement was usually evident, though fibrosis did not change and the number of cases of cloudy swelling increased from 2 to 6.

The biopsy was free from risk in these children when adequate precautions were taken: the only complication of note was a slight emphysema at the puncture site in one case, and this disappeared within 3 hours.

H. J. O'D. Burke-Gaffney

MOULIN, J. Sur quelques cas de scorbut observés chez les nomades du Grand Erg Occidental. [**Some Cases of Scurvy among the Nomads of the Western Grand Erg**] *Arch. Inst. Pasteur d'Algérie.* 1959, June, v. 37, No. 2, 312–14.

MIKEŠ, A. Jetra kod pelagre. [**The Liver in Pellagra**] *Acta Med. Iugoslavica.* 1958, v. 12, No. 3, 320–40, 4 figs. [25 refs.] English summary.

The author has made an investigation of hepatic function in 40 patients suffering from pellagra who were residents of Banja Luka, Yugoslavia, an area in which pellagra is endemic. Hypoproteinaemia was found to be present in 12, hypoalbuminuria in all patients, and hypogammaglobulinaemia in 26 patients. In flocculation tests the percentage of positive results was not greater than the normal frequency and the results were indeterminate in many instances. The serum cholesterol was lowered in 70% of patients, the blood sugar was 105 mgm.% and the sugar tolerance curve was flattened and protracted. The serum iron content was below normal in 61·5% of patients.

Liver biopsy was carried out on 16 patients; the lesions observed included fatty degeneration, round cell infiltration and pigmentation. *D. J. Bauer*

HAEMATOLOGY

JACOB, Gillian F. & SIBTHORPE, Elsie M. **Haematological Values in African Cord Bloods.** *East African Med. J.* 1959, June, v. 36, No. 6, 323–5.

"Results of cord blood haemoglobin, packed cell volume and red blood cell estimations in 100 African infants of the Baganda tribe are presented.

"Comparison with published figures in Europeans and with a small control series of Europeans in Uganda suggests that these figures are somewhat lower in Africans.

"There is no evidence to suggest the reason for this probable difference."

WALSH, R. J., COTTER, Helen & MACINTOSH, N. W. G. **Haemoglobin Values of Natives in the Western Highlands, New Guinea.** *Med. J. Australia.* 1959, June 20, v. 1, No. 25, 834–6, 4 figs. [22 refs.]

"The mean haemoglobin value of 2074 adult male natives resident in the Western Highlands of New Guinea was found to be 17·20 grammes per 100 ml. Analysis of the values in different sub-areas showed a positive correlation between altitude and mean haemoglobin value. The altitudes ranged between 4800 feet and 8250 feet above sea level. A high mean value (15·19 grammes) was also found among 30 adult female natives living at an altitude of 7250 feet."

[See also this *Bulletin*, 1958, v. 55, 803.]

See also p. 1178, WALT, **Anaemia in Kwashiorkor.**

CHATTERJEA, J. B. & RAY, R. N. **Hereditary Spherocytosis.** *J. Indian Med. Ass.* 1959, July 1, v. 33, No. 1, 1–6, 19, 2 figs. on pl. [21 refs.]

"Seven cases of hereditary spherocytosis are reported in detail. All were Indians. Their ages varied from 2½ to 26 years. In one family, there were three brothers who had associated vascular pseudohaemophilia. In every case spherocytosis of varying degree was found in either of the parents. Splenectomy was done in one case with beneficial result."

COHEN, Flossie, ZUELZER, W. W., NEEL, J. V. & ROBINSON, A. R. **Multiple Inherited Erythrocyte Abnormalities in an American Negro Family: Hereditary Spherocytosis, Sickling and Thalassemia.** *Blood.* 1959, July, v. 14, No. 7, 816–27, 2 figs. [18 refs.]

An American Negro family is described in which hereditary spherocytosis, sickling and thalassaemia occur. The father with hereditary spherocytosis and the mother with sickle-cell-thalassaemia have 2 children, both with sickle-cell-thalassaemia, and 2 children who are fully normal. The conclusion drawn is that the type of thalassaemia found in this family is non-allelic with the sickling gene.

The thalassaemia in this particular family differed from that which has been called "classical" thalassaemia by not being associated with a high haemoglobin A_2 fraction. The authors suggest that a high A_2 is especially typical of the thalassaemia of Mediterranean peoples but may often not be present in the thalassaemia of Negroes.

In the third generation the offspring of 2 persons with sickle-cell-spherocytosis could be studied. One of them—the widow of a presumed normal person—also had thalassaemia; the other was the wife of a known normal person. There were children who had either received both the sickle-cell and spherocytosis genes, and others who had received neither. This indicates non-allelism of the genes for spherocytosis and for sickling.

This article is particularly interesting because of its discussion of the problem: "What is thalassaemia?" Hitherto, thalassaemia has been defined as an iron-resistant, hypochromic, micro- and leptocytic haemoglobinopathy.

Is it permissible to restrict this term to those cases which also show an elevation of the A_2 component? There is yet a thalassaemic condition where the gene interacts with those responsible for sickling, haemoglobins C and E, and where in the heterozygote for AS, AC, or AE, it may so modify the haemoglobin pattern that haemoglobin A production is completely suppressed.

H. Lehmann

CHERNOFF, A. I. **The Distribution of the Thalassemia Gene: a Historical Review.** *Blood.* 1959, Aug., v. 14, No. 8, 899–912, 1 fig. [190 refs.]

PEARSON, H. A. & MCFARLAND, W. **Starch Block Electrophoresis of Hemoglobin.** *U.S. Armed Forces Med. J.* 1959, June, v. 10, No. 6, 693–700, 4 figs. [11 refs.]

The diagnosis of thalassaemia is no longer based merely on the examination of the red cell morphology, but also on the measurement of haemoglobin F and on the quantitative determination of haemoglobin A_2. Haemoglobin A_2 is present normally in adult blood but its percentage rarely exceeds 3. In persons with thalassaemia trait, however, the proportion of haemoglobin A_2 is higher. The exact values are given by KUNKEL *et al.* [this *Bulletin*, 1956, v. 53, 488; 1958, v. 55, 309] who state that in normal persons, haemoglobin A_2 amounts to between 1·5% and 3·1%, and that in thalassaemia trait the values are increased to above 3·2%.

To measure such small proportions quantitatively requires a technique such as starch electrophoresis. The technique is basically the same as that of paper electrophoresis but paper is replaced by a starch-block as the supporting medium. This permits a much larger amount of haemoglobin to be applied, and at the end of the electrophoretic run the haemoglobin A_2 fraction can be eluted and measured in the eluate. The same procedure applies to the measurement of the haemoglobin A_1 fraction, and from both values the percentage of haemoglobin A_2 is then calculated.

The present paper describes the procedure of starch electrophoresis in detail as well as the quantitation of the haemoglobin fractions. 3 illustrative cases are detailed.

H. Lehmann

See also p. 1163, CHARMOT & REYNAULD, Relations entre l'ankylostomose et la drépanocytose. **[Relations between Hookworm Disease and Sickling]**

HENDERSON, A. B., CROCKETT, Ethelene J. & WRIGHT, C. H. **Effect of Carbonic Anhydrase Inhibitors on the Course of Sickle-Cell Disease.** *Arch. Intern. Med.* 1959, July, v. 104, No. 1, 68–71. [14 refs.]

"Carbonic anhydrase inhibitors were administered to four adult patients having sickle-cell disease. Periods of observation extended from two hours to seven months. No effect of importance could be noted. Variations in in vivo sickling, erythrocyte count, and sedimentation rate between cells containing oxygenated and reduced hemoglobins were not significant enough to be indicative of value."

[See this *Bulletin*, 1957, v. 54, 1350.]

DEDMON, R. E., EMANUELI, A. & TROBAUGH, F. E., Jr. **Hemolytic Studies in Homozygous Hemoglobin C Disease.** *Amer. J. Clin. Path.* 1959, June, v. 31, No. 6, 487–95, 6 figs. [22 refs.]

"1. Two cases of homozygous hemoglobin C disease are presented along with conditions not reported frequently in association with this entity, namely, Paget's disease of bone and a convulsive disorder.

"2. The hematologic data are discussed with particular reference to autohemolysis and osmotic fragility of the erythrocytes. The authors conclude that autohemolysis studies may be useful in providing basic information with regard to red cell metabolism and perhaps in helping to distinguish between thalassemia minor and iron deficiency. Hemoglobin electrophoresis is the definitive procedure for making the diagnosis of hemoglobin C disease or trait.

"3. Both patients exhibited moderately shortened erythrocyte survival, studied by Cr^{51}-tagged erythrocytes.

"4. This disorder is compatible with a normal and active life span."

WENT, L. N. & MACIVER, J. E. **Sickle-Cell/Haemoglobin-J Disease.** *Brit. Med. J.* 1959, Aug. 8, 138–9, 2 figs.

"A case of sickle-cell/haemoglobin-J disease is reported. The interaction between the genes for haemoglobin S and J is not marked, resulting in a mild well-compensated haemolytic anaemia. Family studies suggest that the haemoglobin J was contributed by a Caucasian from North America."

VENOMS AND ANTIVENENES

DOMERGUE, C. A. Clé de détermination des serpents de Tunisie et Afrique du Nord. [**Key to the Snakes of Tunisia and North Africa**] *Arch. Inst. Pasteur de Tunis.* 1959, June, v. 36, No. 2, 163–72, 9 text figs. & 24 figs. on 16 pls.

DOMERGUE, C. A. Liste des Ophidiens de Tunisie de l'Algérie et du Maroc. [**List of Snakes of Tunisia, Algeria and Morocco**] *Arch. Inst. Pasteur de Tunis.* 1959, June, v. 36, No. 2, 157–61. [15 refs.]

GAIL, R. & RAGEAU, J. Introduction à l'étude des serpents marins (Ophidiens Hydrophiidae) en Nouvelle-Calédonie. [**Introduction to the Study of Sea Snakes (Hydrophiidae) in New Caledonia**] *Bull. Soc. Path. Exot.* 1958, May–June, v. 51, No. 3, 448–59, 13 figs. [26 refs.]

A short account of Hydrophiidae is given and the specimens examined by the authors are listed.

A key to Hydrophiidae is given in detail, based on the characteristics of the ventral scales (dividing the Hydrophiinae and Laticaudinae), the head and body, the nares, and the body and head scales.

A short account of the biology of the snakes follows, and experiments on the effects of various venoms are recorded.

3 genera and 7 species of sea-snakes were identified. The effects on the rat of the venoms of 3 (*Aipysurus laevis*, *Pelamis platurus* and *Laticauda colubrina*) were examined. The first venom was neurotoxic and killed the rat in an hour after artificial biting. The other 2 were inert. Despite the latter results the authors consider that it is probably safer to regard all sea snakes as venomous.

[See also this *Bulletin*, 1957, v. 54, 752.] *B. G. Maegraith*

BJÖRK, W. & BOMAN, H. G. **Fractionation of Venom from the Ringhals Cobra.** *Biochim et Biophys. Acta.* 1959, Aug., v. 34, No. 2, 503–14, 6 figs. [18 refs.]

BALOZET, L. Les antigènes des venins de Cérastes et de Lébétines étudiés par la précipitation en milieu gélifié. [**Antigens of Venoms of** *Cerastes cerastes* **and of** *Vipera lebetina* **Studied by Precipitation in Gel**] *Arch. Inst. Pasteur d'Algérie.* 1959, June, v. 37, No. 2, 292–6, 2 figs. [10 refs.]

BATA, A. & VUKOBRATOVIC, S. Effet et application de l'hypothermie dans les morsures de serpents venimeux. [**Effect and Application of Hypothermia in Cases of Snake Bite**] *Bull. Soc. Path. Exot.* 1958, Nov.–Dec., v. 51, No. 6, 998–1008. [21 refs.]

The effects of cooling in relation to the action on white rats of both sexes of solutions of the venom of *Vipera ammodytes* were studied. The venom was administered by intracardiac, intraperitoneal or subcutaneous route in lethal doses (100% deaths in 48 hours).

General hypothermia was achieved by two methods. (1) The animals were immersed in iced water until the body temperature reached 20°C. They were then withdrawn, after which the temperature continued to fall several degrees. They remained in this state for some 40 minutes. (2) A " cocktail " of sodium thialbarbitone, Largactil [chlorpromazine] and Phenergan [promethazine] was administered. The temperature reached 30°C. in about 1 hour, upon which the animals were packed in ice until a final temperature of 24°C. was reached. They remained in this state for 45 minutes.

Local hypothermia over the site of subcutaneous injection of the venom was obtained by spraying with ethyl chloride.

Intracardiac and intraperitoneal injection of venom in ice-cooled animals was followed by modified symptoms of toxicity but the time of survival was not affected. Intracardiac injection in " cocktailed " animals was also fatal within normal times.

Local cold applied to the sites of subcutaneous injection of venom delayed the time of death, but did not save the animals. Amputation of the tail 4 cm. above the site of subcutaneous injection of venom and 10 minutes after the injection, saved 3 of 10 animals. Amputation of the tail 10 minutes after the immediate application of freezing to the injection site saved 10 out of 10.

The authors conclude that general hypothermia has no effect on the action of viper venom. Local hypothermia is however clearly of value in restricting the absorption of venom from the bite area.

[See also this *Bulletin*, 1953, v. 50, 555; 1957, v. 54, 1119.]

B. G. Maegraith

SCHENONE, H. Estudio de 27 casos de Loxoscelismo. [**A Report on 27 Cases of Loxoscelism**] *Bol. Chileno de Parasit.* 1959, Jan.–Mar., v. 14, No. 1, 7–13, 4 figs. [16 refs.]

The English summary appended to the paper is as follows:—

"1.—27 human cases of arachnidism by *Loxosceles laeta* studied from the clinical, therapeutical and epidemiological standpoint are reported.

"2.—25 cases were of the benign cutaneous type, while the 2 remaining patients presented the more severe and systemic visceral-cutaneous manifestations, death ensuing in one of them.

"3.—The majority of the patients were female with ages ranging from 3 to 72 years.

"4.—Most of the patients had been bitten inside their houses, 17 while sleeping or dressing themselves.

"5.—Local manifestations at the site of venenation were observed in all patients, in a few days evolutioning to a gangrenous spot without lymphatic involvement.

"6.—The antihistaminic drug chlorprophen-pyridamine (Chlor-Trimeton) was administered parenterally as treatment. Local pain and edema were relieved almost immediately upon administration of the drug, a milder evolution of the gangrenous spot being observed when treatment was early started.

"7.—Prevention of the disease is based on an adequate information to the public and appropriate general sanitation measures tending to eliminate spiders."

[See this *Bulletin*, 1957, v. 54, 1121; 1958, v. 55, 212.]

WIENER, S. **Stone-Fish Sting and its Treatment.** *Med. J. Australia.* 1958, Aug. 16, v. 2, No. 7, 218–22, 2 figs. [20 refs.]

Two species of stone-fish, *Synanceja* spp., occur in Australian waters. The author summarizes previous accounts of people receiving injuries from walking on the spines or handling the fish. The clinical picture is dominated by acute local pain and swelling. Cellulitis and sloughing may follow. Fatal stings have been reported. A case history is given as a report from the husband of a woman who received a sting wound on the big toe. Pain was severe within a minute. Within 10 minutes the leg was numb and paralysed to the knee; the pain grew steadily worse. 10 hours later she became semi-conscious and shocked and seemed near death. She recovered slowly.

Many forms of treatment have been recommended. The author recommends immediate tourniquet application, injection of 1 grain emetine along the track of the injury, or simply immersion in hot water. Prophylactic penicillin and tetanus antitoxin should be given against secondary infection and tetanus.

B. G. Maegraith

TOXOPLASMOSIS

STARZYK, J. Badania nad czestością wystepowania toksoplazmozy w województwie krakowskim. [**Investigations on the Incidence Rate of Toxoplasmosis in the Cracow Province**] *Wiadomości Parazytologiczne*. Warsaw. 1959, v. 5, Nos. 2/3, 249–53.

The English summary appended to the paper is as follows:—

"For 3 years investigations on toxoplasmosis are conducted in the Cracow province. They are carried out in various environments, applying Frenkel's and Sabin-Feldman's tests.

"Up till now the following examinations were carried out:

1) 371 persons — employees of 9 slaughter-houses. Positive results with Frenkel's test were obtained in 39%, with Sabin-Feldman's test — in 20·42%.

2) 400 heads of cattle from 11 sheds. S. F. test gave positive results in 24·25%.

3) 121 workers attending cattle. S. F. test, positive results—10·74%.

4) 44 mountaineers engaged in sheep breeding in mountainous regions. S. F. test, positive results — 2·27%.

5) 65 hunters and sanitary controllers of hunting places. S. F. test, positive results — 15·3%.

6) 478 donors at the Blood Transfusion Station in Cracow. S. F. test, positive results — 0·80%.

7) 482 persons originating from three various rural environments. Positive results: 1. S. F. — 15·17%, 2. S. F. — 3·80%, 3. S. F. — 1·49%.

8) 81 wild rats caught in three slaughter-houses. S. F. test, positive results — 10·96%.

9) 50 hens from a little farm in Zywiec. S. F. test, positive results — 0%.

10) 50 doves originating from the Cracow city region. S. F. test, positive results — 2%.

"The aim of our investigations is to give a picture of the occurrence of infections with this protozoon and to discover possible endemic foci of toxoplasmosis. Further — to establish the average of toxoplasmosis incidence in the area of the Cracow province."

ČATAR, G. Badania nad toksoplazmozą w Słowacji. [**Research on Toxoplasmosis in Slovakia**] *Wiadomości Parazytologiczne*. Warsaw. 1959, v. 5, Nos. 2/3, 255–7.

The English summary appended to the paper is as follows:—

"Some investigations on toxoplasmosis carried out in Slovakia were briefly discussed. In a group of 103 women with habitual miscarriages, 50·5% showed positive intradermal reactions with toxoplasmin, and 41·6% positive results in the complement-fixation test. When testing a group of 147 patients suffering from thrombophlebitis, a positive intradermal reaction was found in 68·6% while in the control group—25%. In collective examinations of free living animals, 162 mammals and 24 species of birds were tested for toxoplasmosis. Neither microscopic preparations nor attempts to isolate strains gave positive results."

KAUFMAN, H. E., MELTON, Marjorie L., REMINGTON, J. S. & JACOBS, L. **Strain Differences of** *Toxoplasma gondii*. *J. Parasitology*. 1959, Apr., v. 45, No. 2, 189–90.

The virulence of two strains of *Toxoplasma gondii* was compared in tissue culture. 200,000 RH organisms and 1 million 113-CE organisms were inoculated into monkey kidney tissue culture; the inocula were washed off after 3 hours and the tubes were incubated in stationary racks for 24½ hours, when the material was stained and the density of infection was estimated.

The RH strain showed over 3 times as many organisms in each infected cell as the other strain; and the cell sheet was destroyed in 4 days instead of 12 days or longer. If the cultures were maintained in roller drums, the degree of invasion was reduced to a quarter, presumably because attachment and penetration were interfered with. Tissue cultures of strain 113-CE (and another avirulent strain—721) often lasted for a long time, with the development of a "chronic" infection, light in intensity, but found to be viable when inoculated into mice. It is suggested that a balance was maintained between host cell and parasite, with the latter almost dormant. *P. C. C. Garnham*

LUDVÍK, J. **Morphology of** *Toxoplasma gondii* **in Electron Microscope.** *Věstn. Českoslov. Zool. Spol.* Prague. 1958, v. 22, No. 2, 130–36, 1 text fig. & 17 figs. on 4 pls. [16 refs.]

In a previous paper [this *Bulletin*, 1956, v. 53, 1167] the author described the appearance of *Toxoplasma gondii* in total preparations examined by electron microscopy. In the present paper he deals with the cytology of this parasite as seen in thin sections (0·02–0·03 μ) prepared from the sediment of centrifuged peritoneal exudate of infected mice, and examined under an electron microscope. The structure of the parasite, illustrated by a series of micrographs and represented schematically, is as follows. The body is oval and slightly bent, with a pointed anterior end and rounded posterior end. It is covered by a pellicle (30–50 mμ thick) consisting of 2 layers. The anterior end contains a special organelle, the conoid, consisting of a polar ring (0·25–0·30 μ in diameter) and an interior cone (0·2–0·25 μ in diameter) lying in the cytoplasm. From the ring are given off 12–16 radial rib-like strands running on the surface of the pellicle to the middle of the body and representing supporting structures; while a bunch of about 15 club-shaped fibres or toxonemes arise from the centre of the conoid and terminate within the cytoplasm in the nuclear region.

The nucleus lies in the middle of the body, and measures 1–2 μ; it is covered by a thin membrane (15–30 mμ) and contains a large (0·5 μ) nucleolus. Other cell inclusions include a group of hollow mitochondria (0·13–0·15 μ in diameter) in the posterior part of the body, the Golgi apparatus composed of fine fibres (15–20 mμ) on the anterior surface of the nucleus, and an endoplasmic reticulum consisting of fine long tubes (15 mμ thick).

Toxoplasma apparently multiplies by the formation of 2 daughter individuals within the parental body.

The author suggests that the parasite penetrates into the host-cell by attaching itself with the polar ring and boring its way with the help of the radial bands (possibly representing myofibrils), while the function of the toxonemes is

supposed to be secretory. The secretion might be adhesive, serving to attach the parasite to the host-cell, or enzymatic, in assimilating its contents, or both.

C. A. Hoare

ANGELILLO, B. & MANDRAS, A. Sull'impiego dell'emoagglutinazione nella diagnosi di toxoplasmosi. [**The Employment of the Haemagglutination Test in the Diagnosis of Toxoplasmosis**] *Igiene Moderna.* 1959, v. 52, Nos. 3/4, 175–81. [11 refs.] English summary (5 lines).

The Sabin and Feldman dye test, the complement-fixation test and haemagglutination were tested by the authors on 75 presumed healthy persons, and 55 persons known to be infected with toxoplasms. Of the healthy persons examined, 3 were positive to the dye test and 3 to the CF test. 5 were positive to the HA test (3 of these to a titre of only 1 in 10). 48 of the infected group were positive to dye, 46 to CF, and 49 to HA (9 had a titre of 1 in 10).

As the percentages positive in the 55 affected persons were practically the same the author considers that the tests ran practically parallel.

[3 of the healthy persons showed a haemagglutination titre of 1 in 10, and 1 was positive to 1 in 160, while 1 of the known affected people was negative to all 3 tests and 3 negative to 2. The significance of the 1 in 10 + HA might require further consideration.]

W. K. Dunscombe

KABELITZ, H. J. Abdominelle Symptome bei postnatal erworbener Toxoplasmose. [**Abdominal Symptoms of Postnatally Acquired Toxoplasmosis**] *Deut. med. Woch.* 1959, July 31, v. 84, No. 31, 1379–84, 1404. [17 refs.]

The English summary appended to the paper is as follows:—

"As observed in 52 personal cases, post-natally acquired toxoplasmosis usually runs a chronic course without fever and with symptoms which are predominantly localized to the abdominal organs. Initial lymphadenitis is rare. Abdominal involvement generally consists of hepato- and splenomegaly, prolonged bilirubinaemia, digestive disorders with tendency towards diarrhoea, and enlargement of the mesenteric lymph nodes with pain in the mid and lower abdomen. Peripheral leukopenia may persist for months. Lymphocytosis only occurs in the lymphadenitic form. The eyes are rarely involved. Loss of weight is common and considerable. Active toxoplasmosis is diagnosed with the Sabin-Feldman test and the complement-fixation reaction: Fresh infection is characterized by at first a rising and then a falling titre. Eight case reports are presented in detail: The Sabin-Feldman test varied maximally between 1:64,000 and 1:64 (Case 2), and minimally between 1:64,000 and 1:4,000 (Case 8)."

VAN DEN AKKER, S., BOOL, P. H. & SPITS-ESHUIS, W. C. Toxoplasmosis bij een hond. [**Toxoplasmosis in a Dog**] *Tijdschr. v. Diergeneesk.* 1959, July 15, v. 14, No. 84, 767–73, 4 figs. on 2 pls.

The English summary appended to the paper is as follows:—

"In view of the fact that *Toxoplasma gondii* has been isolated from a dog and from a monkey (*Macacus tantalus*), the diagnosis of toxoplasmosis is

critically considered. A 4-year-old German sheep-dog showing pulmonary symptoms was found to be affected with catarrhal bronchopneumonia. A large number of mononuclear cells in the alveoli were charged with parasites, defined as *Toxoplasma gondii* on examination of the smears, the identity being determined by passages through mice.

"Toxoplasma was isolated from the brain of a monkey (*Macacus tantalus*) with chronic diarrhoea, the titre as determined in the Sabin-Feldman test being 1 : 512 and the complement fixation test titre being 1 : 32.

"Macroscopical and microscopical pathologic-anatomical examination, however, was negative."

JONES, Frances E., MELTON, Marjorie L., LUNDE, M. N., EYLES, D. E. & JACOBS, L. **Experimental Toxoplasmosis in Chickens.** *J. Parasitology.* 1959, Feb., v. 45, No 1, 31–7. [12 refs.]

Since the domestic fowl may be spontaneously infected with *Toxoplasma gondii* and in view of its possible role as a source of human infection, the authors have carried out a comprehensive study of experimental toxoplasmosis in these birds. For this purpose chickens were inoculated by various routes with different doses of parasites (300–100,000,000) obtained from the peritoneal exudates of infected mice or from chick embryos. For the study of parasitaemia and localization of toxoplasms in the chickens, their blood and tissue suspensions, respectively, were inoculated intraperitoneally into mice. In addition, daily observations were made on the clinical manifestations of the disease.

The experiments have shown that fowls are very tolerant to toxoplasmosis, since only large inocula (1×10^6 parasites) produced disease with fatal results in adult birds, while young chickens survived infection produced by inocula that are fatal to laboratory rodents. Evidence of parasitaemia was obtained 2–3 days after inoculation, but it only occasionally persisted over 2 weeks. It was also found that the infection cleared itself spontaneously after about 40 days. Attempts to lower the resistance of the birds by changes in diet and by administration of cortisone were unsuccessful. There was also no evidence to show that human beings might contract toxoplasmosis from eating the flesh of infected chickens, since the parasites rapidly disappeared from the muscles of infected birds. The dye test revealed only very low levels of antibody in such birds, therefore positive reactions obtained in the course of surveys might only indicate the presence of active or recent infection. For all these reasons, chickens are not suitable experimental hosts for chemotherapeutic tests.

C. A. Hoare

BEVERLEY, J. K. A. **Congenital Transmission of Toxoplasmosis through Successive Generations of Mice.** [Correspondence.] *Nature.* 1959, May 9, v. 183, 1348–9.

Pregnant Swiss mice were inoculated subcutaneously with cysts of a rabbit strain of *Toxoplasma gondii* of low virulence. Congenital transmission to the offspring occurred in all instances; 6 of the latter were mated and transmission to the third generation occurred; continuation in the fourth and fifth generations then took place. The presence of infection in a litter was determined by

finding cysts in the brains of males 6 weeks old. Infection must be transplacental because surgically removed foetuses were found to be infected. Infection *via* the milk was observed, but not by droplet, faeces or urine.

P. C. C. Garnham

ARMSTRONG, J. A. & FULTON, J. D. **Observations on the Pathology of Toxoplasmosis in the Cotton Rat.** *Brit. J. Exper. Path.* 1959, June, v. 40, No. 3, 225–31, 9 figs. on 2 pls. [10 refs.]

Young adult cotton rats were inoculated intraperitoneally with the RH strain of *Toxoplasma gondii.* 3 days later the animals became ill and they were killed on that day or the following one. The organs were fixed and prepared in various ways for observation of the pathological changes.

An unusual penile secretion condensing into a rubbery mass up to an inch long was found; it extended up the urethra and into the bladder, and was apparently produced by the inflammatory reaction in the pelvic accessory glands (the condition was also observed in 20% of infected adult white mice). The skin on the back and on the abdomen was swollen, and the subcutaneous tissue had a jelly-like consistency.

The histological appearances showed an intense inflammatory reaction of the mesodermal elements of the various organs and tissues, accompanied by invasions with the organism (easily visible when stained by acridine orange and examined by fluorescent microscopy). In the pelvic viscera, the cells had large oval nuclei and an eosinophilic cytoplasm which was often vacuolated or foamy. The epithelium in all tissues, including the liver, was free from parasites, and no organisms were found in the central nervous system. An interesting condition was seen in the liver, where periportal vacuolation of the parenchyma was found to be due to accumulation of intracellular fat; this condition was apparently due to toxins produced by the parasite, because inoculation of ruptured organisms, or of the supernatant of centrifuged peritoneal exudate gave rise to the same appearance (on the second to fourth days after inoculation).

The pathology of the infection in cotton rats is thus seen to differ in important respects from that of mice, *Mastomys* or other rodents, in which, for instance, invasion of the parenchyma cells of the liver is a common feature.

P. C. C. Garnham

DERMATOLOGY AND FUNGUS DISEASES

HARTER, P. *Dermatosis papulosa nigra* en Afrique noire. [**Dermatosis Papulosa Nigra in Africans**] *Bull. Soc. Path. Exot.* 1958, May–June, v. 51, No. 3, 341–5, 4 figs. on 2 pls.

This disorder is confined to coloured races. It consists of hyperpigmented papules, some discrete others confluent. The papules are flat or rounded with

a plane surface and sharply demarcated edge; they are of variable size up to a maximum of 3 or 4 millimetres.

Areas rich in seborrhoeic glands tend to be principally affected, particularly the face, where they are seen on the cheeks, temporomalar areas, the eyelids, forehead and behind the labial fold. The nose, upper lip, scalp and ears are unaffected. The lesions never clear spontaneously but do, in fact, get larger and more numerous with age.

2 particular varieties are common:—a comedo-like form in which an orifice can be seen on the papule and white fatty material can be expressed from it; a verrucose form may occur on the lower lid and sometimes grows into a papillomatous tumour.

Histologically hyperpigmentation occurs in the basal layer which forms projections into the dermis. There is a certain amount of hyperkeratosis. Horny cysts are common, some forming on the surface, others forming at the base of one of the digitate processes.

In differential diagnosis it is important to distinguish plane warts, seborrhoeic warts and adenoma sebaceum. *H. T. H. Wilson*

Fernández Baquero, G. & Trespalacios, F. Piedra. Primer caso observado en Cuba. [**First Case of Piedra observed in Cuba**] *Bol. Soc. Cubana de Dermat. y Sifil.* 1959, Mar., v. 16, No. 1, 21–7, 6 figs. [17 refs.]

Kaplan, W. **The Occurrence of Black Piedra in Primate Pelts.** *Trop. & Geograph. Med.* Amsterdam. 1959, June, v. 11, No. 2, 115–26, 8 figs. [13 refs.]

"The results of a study to determine the occurrence of piedra in primate pelts are presented and discussed. Four hundred and thirty-eight museum primate pelts were examined and of this number, 195 (44·5%) were found to have black piedra.

"Of 94 Asian primate skins studied, 57 (60·0%) showed this disorder, as did 58 (28·7%) of 202 African and 83 (76·1%) of 109 New World animal skins. Only 2 of 33 (6%) of the pelts obtained from New York zoological park primates were found to be affected.

"With the exception of the primitive Lorisoids, skins from primates grouped in nearly all the major divisions of this zoological order were found to have this disorder to varying extents.

"The findings of this study established the occurrence of black piedra in hairs of a diversity of primate species, in addition to man, and suggest the existence of a widespread reservoir of infection in the forests of tropical and semi-tropical Africa, Asia and Latin America."

Brygoo, E. R. & Ratovondrahety. Sur huit cas de chromoblastomycose diagnostiques à Antalaha. [**Eight Cases of Chromoblastomycosis diagnosed at Antalaha (Madagascar)**] *Arch. Inst. Pasteur de Madagascar.* 1959, v. 27, 71–4.

CORREA, P. Blastomicosis queloidiana. [**Keloid Blastomycosis**] *Rev. Latinoamer. Anatom. Patol.* Caracas. 1958, July–Dec., v. 2, No. 2, 139–43, 4 figs. on 2 pls.

The English summary appended to the paper is as follows:—

"A new case is presented of keloid blastomycosis or Lobo's disease. It represents the first case found in Colombia, and the second case outside the Amazon Basin. The clinicopathologic and mycologic aspects of the disease are discussed as well as the similarities and differences with South American blastomycosis."

AJELLO, L., WALLS, K., MOORE, Jane C. & FALCONE, R. **Rapid Production of Complement Fixation Antigens for Systemic Mycotic Diseases. I. Coccidioidin: Influence of Media and Mechanical Agitation on its Development.** *J. Bacteriology.* 1959, June, v. 77, No. 6, 753–6.

In the United States where systemic diseases due to fungi constitute a widespread and serious problem it is important to be able to perform reliable diagnostic and prognostic tests. This is best accomplished by complement-fixation tests, for which large stocks of antigen are required. In this paper the authors describe a simple, rapid and reproducible method whereby the antigen coccidioidin may be prepared.

For the production of the antigen 4 strains of *Coccidioides immitis* were used. These were grown separately in flasks on each of 5 different culture media. Half of these flasks were kept stationary and half were kept agitated. At the end of the required period of growth the cultures were killed and filtered. In order to provide greater antigenic coverage the supernatant fluids of the cultures of all 4 strains grown on a like medium under like conditions were pooled.

It was found that the best of the 5 media used for the production of the antigen was neopeptone dialysate [EVANS and KESSEL, *Bull. Hyg.*, 1952, v. 27, 206] when this was kept agitated. It had the following composition: neopeptone, 1 part (60 gm. per litre of water) held at 70–80°C. for 6–8 hours and overnight in a cold room at 4°C.; distilled water, 2 parts, and glucose, 2%.

The 50% haemolytic end point complement-fixation test previously described by SCHUBERT *et al.* [*Bull. Hyg.*, 1955, v. 30, 975] for the evaluation of histoplasmosis and yeast-phase antigens from a strain of *Histoplasma capsulatum* was used throughout the present work, while sera from culturally proved cases of coccidioidomycosis were used in evaluating the experimental antigens. The highest reactivity was reached with neopeptone dialysate (agitated) after three weeks' growth. Maximum activity was reached with this medium at 1 in 8 dilution, which proved it to be equal in activity with standard C. E. Smith antigen [this *Bulletin*, 1948, v. 45, 929; 1951, v. 48, 73], but it was found to have the further advantage that it was free of anti-complementary activity and did not produce skin test reactivity. *C. J. La Touche*

TROPICAL ULCER

TRIPODI, P. & CAPOCACCIA, L. Diagnosi etiologica e clinica delle più comuni ulcere della gamba cosmopolite e tropicale. [**Aetiological and Clinical Diagnosis of the Commoner Cosmopolitan and Tropical Ulcers of the Leg**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1958, Nov. & Dec., v. 39, Nos. 11 & 12, 709–22 ; 725–92. [Numerous refs.]

O'CONNOR, H. & COURBIL, J. Des ulcères phagédéniques et de leurs complications (à propos de 50 cas hospitalisés, dont 30 cancers). [**Tropical Ulcers and their Complications. An Account of 50 Hospital Cases including 30 Cases of Malignant Growths**] *Méd. Trop.* Marseilles. 1958, May–June, v. 18, No. 3, 443–59, 5 figs.

Tropical ulcer may be complicated by severe scarring and bone involvement, by gangrene or by the development of carcinoma in the site of the ulcer.

Details of examples of each of these complications are given. The most important contribution refers to the development of new growths in the ulcerated region. The authors give details of 30 patients, 29 of whom developed carcinoma, 1 only developed sarcoma. Metastasis in the local glands was recorded in 5 cases. There were no pulmonary metastases. Amputation may be necessary in cases with cancerous complications. *B. G. Maegraith*

MISCELLANEOUS DISEASES

FELSANI, F. Osservazioni nosografiche nel bassopiano del Yemen. [**Diseases of the Yemeni Lowlands**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1959, May, v. 40, No. 5, 239–68. [28 refs.] English summary (5 lines).

The author, who was Director of the Medical Division of the Royal Hospital at Hodeidah (which is a port on the Red Sea not far from Perim) from 1952 to 1957, gives a most interesting account of the geography, climatic conditions, and habits of the people of the Yemen lowlands and their diseases. The population of the area is between $1\frac{1}{2}$ and 2 millions and the climate which is hot and humid is affected greatly by both the south-west and north-east monsoons. Among adults the consumption of Qat (*Catha edulis*) is almost universal. The leaves contain 3 alkaloids ; the principal, d-nor-isoephedrine, has an excitant action on the central nervous system.

In Hodeidah the standard of living and of hygiene is relatively high but infant mortality is also high owing largely to irrational feeding. Whooping-cough is epidemic each year but prophylactic vaccination has been practised in the last few years. Diphtheria also occurs, and here also vaccination has been carried out in the last 2 years. In general, the principal diseases are pulmonary tuberculosis which is widely diffused, schistosomiasis, mostly due to *Schistosoma mansoni* (*S. haematobium* infections are extremely common in the uplands), malaria, amoebiasis, bronchial asthma, and syphilis. *Ascaris* infection is also

common. The Arab race seems to have a predisposition to diabetes and urolithiasis, the calculi being chiefly oxalate. The predisposition to bladder stone in males is considered to be due to the habit of micturating in the squatting position with resulting incomplete emptying of the bladder. Trachoma affects about 90% of the inhabitants. Special mention is made of the number of cases of cirrhosis of the liver accompanied in each instance by marked splenomegaly. The author considers that this condition is definitely associated with malaria, though this is due to *Plasmodium falciparum*. Arterial hypertension is very rarely seen and he has never seen a case of rabies. Diseases of the digestive system are common and a number of cases of atony of the gall-bladder, possibly due to the consumption of Qat, have been reported on X-ray examination.

[The author is obviously an acute observer and his account is most instructive. It might be objected, however, that conditions at Hodeidah are hardly representative, at least in the last few years, by reason of the foreign technical aid given in constructing a modern port there. The high incidence of bronchial asthma and the absence of rabies are interesting but identification of the malaria vector would have been helpful.] *W. K. Dunscombe*

VERVOORN, J. D. & DE JAGER, H. **Rhinoscleroma in Ghana. Report on a Case.** *Trop. & Geograph. Med.* Amsterdam. 1959, June, v. 11, No. 2, 182–5, 3 figs. & 1 map.

"Description of the first case of rhinoscleroma in Ghana. Treatment with streptomycin 1 g daily gave good results."

VAZ, J. M. Corps chromatiniques dans les bactéries du genre *Malleomyces*. [**Chromatin Bodies in** *Malleomyces*] *Cadernos Cient.* Lisbon. 1959, Mar., v. 5, No. 3, 393–6, 2 figs.

The English summary appended to the paper is as follows:—

"The presence of chromatin bodies were shown in the two species of the genus *Malleomyces*: *M. mallei* and *M. pseudomallei*. For that purpose the author used the method developed by Robinow on that first described by Pikarski.

"We can then place *M. mallei* and *M. pseudomallei* amongst the great number of bacteria in which those chromatin bodies were already known."

V. HOLT, L.; V. HOLT, C.; BENEDICT, I. Biochemie des Hypoglycins A. 1. Die Wirkung des Riboflavins auf den Hypoglycineffekt. [**The Biochemistry of Hypoglycin A. I. The Effect of Riboflavin on the Action of Hypoglycin**] [V. HOLT & V. HOLT]. *Biochem Ztschr.* 1959, v. 331, No. 5, 421–9, 7 figs. [20 refs.] II. Der Einfluss des Hypoglycins auf die Oxydation von Glucose und Fettsäuren. [**The Effect of Hypoglycin on the Oxidation of Glucose and Fatty Acids**] [V. HOLT, C. & BENEDICT]. *Ibid.*, 430–35, 4 figs.

The English summaries appended to the paper are as follows:—

i. "Repeated administration of β-Methylenecyclopropyl-α-amino-propionic acid (hypoglycin A) causes a temporary reduction of glycosuria in the alloxan

diabetic rat. This effect of hypoglycin is dependent on the riboflavin content of the diet. Pre-treatment with riboflavin decreases the mortality of mice following repeated administrations of hypoglycin and at the same time prevented the fatty infiltration of the liver observed when the amino acid alone is given."

ii. "β-Methylenecyclopropyl-α-amino-propionic acid (hypoglycin A) causes an increase in oxidation of uniformly labeled ^{14}C-glucose to $^{14}CO_2$ in normal and alloxan diabetic rats to about twice the values observed in untreated animals. At the same time the oxidation of 1-^{14}C-labeled palmitate is decreased to about one half, while that of 1-^{14}C-capronate remains unchanged."

BENNETT, J. H., RHODES, F. A. & ROBSON, H. N. **A Possible Genetic Basis for Kuru.** *Amer. J. Human Genetics.* 1959, June, v. 11, No. 2, Pt. 1, 169–87, 6 figs. [10 refs.]

See also this *Bulletin,* 1959, v. 56, 565.

LAHA, P. N. **Intrapleural Pressure in Tropical Eosinophilia.** *J. Ass. Physicians India.* 1959, July, v. 7, No. 4, 320–23.

"A study has been made of intrapleural pressure in 15 cases of tropical eosinophilia.

"The intrapleural pressure has been found to be within the normal range in 13 out of 15 cases. In 2 out of 15 cases the intrapleural pressure has been found to be out of normal range. The cause for the said abnormality is emphysema—a complication of tropical eosinophilia. No correlation has been found between the total eosinophil and white cell counts, and the duration of the illness with the intrapleural pressure in tropical eosinophilia.

"It is concluded that the pathology operating in tropical eosinophilia does not interfere with the physiology governing the maintenance of normal intrapleural pressure, except when emphysema sets in as a complication of the disease."

BHARADWAJ, T. P., GAITONDE, B. B. & JHALA, H. I. **Histamine and Tropical Eosinophilia.** *Indian J. Med. Res.* 1959, July, v. 47, No. 4, 377–81. [25 refs.]

"1. Studies on total eosinophil and basophil counts and histamine values of blood of 10 normals and 16 patients of tropical eosinophilia are presented.

"2. Patients had higher eosinophil and basophil counts than normals, although basophil count was only slightly higher.

"3. The histamine content in normal bloods was found comparable to those reported by others. The histamine content in patients' blood was insignificantly higher as compared to normal. In quite a few, values were within normal range. Histamine content per eosinophil appear to be lesser in patients than in normals.

"4. Theoretical implications and further suggestions are discussed."

BHARADWAJ, T. P. & JHALA, H. I. **Studies on the Disappearance of Infused Hydrocortisone from the Plasma of Normal Subjects and of Tropical Eosinophilia Patients.** *Ann. Biochem. & Exper. Med.* Calcutta. 1959, Feb., v. 19, No. 2, 51–6, 2 figs. [15 refs.]

It has been found that the plasma of patients with tropical eosinophilia is deficient in 17-hydroxysteroids (Bharadwaj *et al.*, *Indian J. Path. Bact.*, 1958, v. 1, 226). The present paper describes an attempt to discover whether this is due to a lower rate of their production by the suprarenal gland or to increased removal.

50 mgm. hydrocortisone were infused into 20 normal people and 20 patients with tropical eosinophilia. Blood was collected at the beginning, and at the end of the infusion after about 30 minutes, and also 2½ hours after the infusion had been completed. There was a significant decrease in the rate of disappearance of 17-hydroxysteroids from the plasma of the patients, which indicates that the lower level of corticoids in their blood was due to a lower rate of production. In 9 of the patients liver function tests were performed and showed a mild but definite impairment. *H. Lehmann*

TURNER, P. P. & HURLEY, D. W. H. **Cushing's Syndrome treated by Bilateral Subtotal Adrenalectomy.** *East African Med. J.* 1959, June, v. 36, No. 6, 314–19, 2 figs. [19 refs.]

A case in a Kikuyu boy. It is believed to be the first case of this endocrine disease recorded in an East African.

PARASITOLOGY: GENERAL

PAWŁOWSKI, Z. **A Review of the Accomplishment of the Polish Medical Parasitology in the Past Two Years 1956–1958.** *Wiadomości Parazytologiczne.* Warsaw. 1959, v. 5, Nos. 2/3, 107–16. [Fuller version in Polish 87–106. (126 refs.).]

ZARNOWSKI, E. **A Survey of the Achievements in the Polish Veterinary Parasitology in the Two Past Years (1956–1958).** *Wiadomości Parazytologiczne.* Warsaw. 1959, v. 5, Nos. 2/3, 134–9. [Fuller version in Polish 117–34.]

G. E. N. Caracas. 1958, Apr.–June, v. 12, No. 4, 31–244, illustrated. [Numerous refs.] III Jornadas Venezolanas de Gastroenterologia, Caracas, Venezuela, 8 & 9 May 1958. [**3rd Venezuelan Conference on Gastroenterology**]

This number of the official organ of the Venezuelan Society of Gastroenterology is devoted almost entirely to the Congress held in Caracas in May

1958. The Congress was in 4 parts: (1) a paper on anatomical and clinical features of the liver in schistosomiasis in Venezuela, (2) 7 papers on surgery of the biliary tract, (3) 3 papers on cancer of the liver and (4) a symposium of 10 papers on parasitic infections.

Readers of this *Bulletin* will be familiar with much of the subject matter of parts (1) and (4) in which they will be chiefly interested. The paper on the liver changes in schistosomiasis is by Dr. Felix PIFANO and his colleagues. The symposium on parasitic infections covers hydatid disease of the liver, enterobiasis, trichuriasis, giardiasis and other flagellates, diagnosis and treatment of taeniasis, strongyloidiasis, radio-active isotopes in the study of ankylostome anaemia, and recent advances in the diagnosis and treatment of ascariasis, of amoebiasis and schistosomiasis. *H. J. O'D. Burke-Gaffney*

CARLI, G. & MAMMINI, P. Rilievi sulla incidenza delle parassitosi intestinali in un gruppo di studenti dell'Ateneo Pisano. [**The Incidence of Intestinal Parasitism in a Group of Students of the Pisa University**] *Riv. di Parassit.* Rome. 1959, June, v. 20, No. 2, 73–8. [11 refs.]

The English summary appended to the paper is as follows:—

"Research performed on the incidence of intestinal parasitism in a group of 550 students of the University of Pisa showed that 52.2% of those examined were parasitised. The incidence of infection with protozoa was 40.9% and that with helminths 20.8%. Mixed parasitosis by protozoa and helminths was present in 9.3% of the subjects.

"Infection with *Entamoeba histolytica* was more frequent amongst students from southern Italy (3.3%) than amongst those from central Italy (1.1%) or northern Italy (0%). The incidence of this parasite amongst foreign students, mainly of Greek nationality, was 11.3%.

"Infections with *Endolimax nana* (24.2%) and *Giardia intestinalis* (10.5%) were also present with marked frequency and these can sometimes be the cause of more or less marked disturbances.

"Attention is drawn to the utility of the preventive medicine measures developed in this field by the organisation of the University of Pisa."

PACHECO DE FIGUEIREDO, J. M. **Contribution to the Study of Intestinal Parasitosis in Goa. Some Clinical and Laboratorial Data.** *Arquivos da Escola Méd.-Cirurg. de Goa.* Ser. A. 1958, No. 31, 38–46.

Findings in previous surveys of intestinal parasitosis in Goa are compared with those obtained by the author. Ascariasis has varied from 34·2% to 75%, ankylostomiasis (*Necator americanus*) from 14·6% to 32% and amoebiasis from 7·1% to 16·2% [disregarding a higher figure for "amoeba" in another series].

Charcot-Leyden crystals were found in 6%, 6·5% and 3·8% in different series. Out of 82 persons in the author's series whose stools contained crystals 19, *i.e.* 23%, harboured *Entamoeba histolytica*; of 346 persons found to be harbouring *E. histolytica* 5·5% had Charcot-Leyden crystals. Out of 2,136 patients with amoebiasis, hepatic abscess occurred in 27 of whom 21 were male. Ankylostomiasis and amoebiasis may be associated with duodenal ulcer. Anaemia, often extreme, and hypo- and avitaminosis are usually the main symptoms. *B. B. Waddy*

FRAGA DE AZEVEDO, J., GÂNDARA, A. F. & FERREIRA, A. P. Estudo sobre a incidência das parasitoses intestinais na Província de Timor. [**The Incidence of Intestinal Parasites in Timor**] *Anais Inst. Med. Trop.* Lisbon. 1958, Mar., v. 15, No. 1, 71–87, 3 figs. [31 refs.]

The English summary appended to the paper is as follows:—

"In 776 persons on Portuguese Timor, the majority (640) between 7 and 14 years of age, the study on distribution and incidence of intestinal parasitoses, with regard to helminths, has shown that their infections rates varied according to the places between the following limits:

Ascaris lumbricoides, between 5 and 93·7%;
Ancylostomidae, between 2·5 and 70%;
Tricocephalus dispar, between 1·5 and 50%;
Enterobius vermicularis, between 1·5 and 30%.

"The rates of the infection average were for all the territory the following, respectively: 24·4%, 8·3%, 5·6 and 0·7%.

"Referring to the protozoa, only the *Entamoeba histolytica* and the *Giardia lamblia* are mentioned, whose infection rates are 4·5 and 10·7% and 1·5 and 5·9% for the two places where each parasite was found.

"Although the writers sometimes noticed differences in the incidence according to the racial divisions, such differences did not appear to have any significance.

"Some increase in the incidence of the helminths is noted with the altitude, but so far we cannot give a full explanation."

HAMPERL, H. La neumonia a neumocistis y la historia de su descubrimiento. [*Pneumocystis* **Pneumonia and the History of its Discovery**] *Rev. Latinoamer. Anatom. Patol.* Caracas. 1958, July–Dec., v. 2, No. 2, 155–62. [13 refs.] English summary.

REIF, A. & SANDBANK, A. [**Pneumonia due to** *Pneumocystis carinii*] *Harefuah*. Jerusalem. 1959, July 1, v. 57, No. 1 [In Hebrew 3–4, 4 figs. on 2 pls. (38 refs.) English summary 5.]

The English summary appended to the paper is as follows:—

"This is the first report on 8 cases of Pneumonia in which Pneumocystis Carinii (P. C.) was found in this country. This disease is well known in Central and Western Europe. P. C. causes an interstitial pneumonia, the infiltrate being rich in plasma cells.

"The clinical picture is characterised by a triad of progressive cyanosis, dyspnea and tachypnea. The main victims of the disease are premature and dystrophic infants, the age of our cases varied from 2–3 months, three of them being premature. Out of our patients six had a history of serious illness in the past, and needed hospitalization. All of them died of respiratory insufficiency, their illness lasting 2–22 days.

"The pathological changes in the lungs were similar in all our cases, the macroscopic picture being non-specific, and the microscopic one representing an interstitial pneumonia. The infiltrate consisted of lymphocytes, histocytes and

areas rich in plasma cells. In the alveola the parasites were found in both reticular and cystic forms."

SHELDON, W. H. **Experimental Pulmonary** *Pneumocystis carinii* **Infection in Rabbits.** *J. Exper. Med.* 1959, July 1, v. 110, No. 1, 147–60, 10 figs. on 5 pls. [20 refs.]

"Moderate to marked interstitial pneumonitis with many *Pneumocystis* organisms was found in rabbits treated with cortisone and antibiotics and instilled intranasally with a suspension of lung tissue from either a patient or a rabbit with this infection. Organisms and pulmonary lesions of similar severity and frequency were present in controls treated in the same manner but instilled with either saline or a boiled suspension of normal human lung tissue. The administration of antibiotics and infected rabbit lung suspension only produced less marked lung changes with fewer organisms. Rare organisms and minute foci of pneumonitis were encountered in normal rabbits which had received neither hormone, antibiotics, nor inoculum.

"The pulmonary lesions in the cortisone-treated rabbits resembled closely the findings in patients with the subclinical form of *Pneumocystis* pneumonitis. They did not reproduce the massive lesions of widespread *Pneumocystis* pneumonia in infants.

"The findings indicate that latent pulmonary *Pneumocystis* infection was widespread in these rabbits but do not establish the transmission of the disease. The activation of latent infection was dependent on an impairment of host resistance which in these experiments was produced most effectively by the administration of cortisone. The differences between the experimental lesions and those of typical *Pneumocystis* pneumonia in infants suggest that in man an unknown defect of host defenses other than that induced by prolonged hormone administration accounts for the increased susceptibility to the infection. It is concluded that in the presence of widespread latent *Pneumocystis* infection the development of active disease is a manifestation of altered host resistance."

TANI, T. & TAKANO, S. **Prevention of** *Borrelia duttonii, Trypanosoma gambiense, Spirillum minus* **and** *Treponema pallidum* **Infections Conveyable through Transfusion.** *Japanese J. Med. Sci. & Biol.* 1958, Dec., v. 11, No. 6, 407–13. [13 refs.]

The danger of acquiring disease by blood transfusion has long been recognized and the present investigation deals with the method of preventing infection by the organisms named in the title through the use of chemotherapeutic agents. The parasites were maintained in mice by blood inoculation, except for *Treponema pallidum* which was obtained from rabbit testes. The infective dose in mice for each parasite was determined by intraperitoneal inoculation, except in the case of *T. pallidum* for which rabbits were used and received intradermal inoculations. The toxicity of drugs was determined in mice by intravenous inoculation and the results are summarized in tables.

The drugs used were Mapharside, salvarsan, penicillin, Achromycin [tetracycline], Terramycin [oxytetracycline], chloramphenicol and streptomycin.

Their prophylactic effect was determined by mixing a known number of parasites with serial dilutions of drugs followed by inoculation of the host animal. In the case of syphilis it was found that 3 mgm. Mapharside added to 100 cc. blood containing *T. pallidum,* when left for 15 minutes at 23°C., could prevent infection. Data for the other drugs are included in the text. *J. D. Fulton*

ENTOMOLOGY AND INSECTICIDES: GENERAL ZOOLOGY

[Papers on the toxic effects of insecticides in man are abstracted in the *Bulletin of Hygiene* under the general heading of Occupational Hygiene and Toxicology.]

FURTUNESCU, G. Cages pliantes pour le transport des culicidés et autres diptères. [**Flexible Cages for the Transport of Mosquitoes and Other Diptera**] *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 5, 1007–9, 2 figs.

ŁUKASIAK, J. Wystepowanie komarów kłujących we wschodniej cześci Puszczy Kampinoskìej. [**Appearance of Stinging Gnats in the Eastern Part of Kampinos Wilderness**] *Acta Parasitologica Polonica.* Warsaw. 1958, Apr. 4, v. 7, Nos. 13/22, 307–14, 2 charts.

The English summary appended to the paper is as follows:—

"The author carried out his investigations in the biggest forest area near Warsaw, i.e. in the Kampinos Wilderness which is distinguished by specific biotypes, representing seats of the proper fauna of forest and meadow gnats.

"The investigations were carried out in the deep situated areas of the eastern part of the Wilderness, and the chief places of catches of gnats were swampy areas overgrown with alder-wood, horn-beam, oak, pine, birch, spindel-tree, hazel-tree and other small plants.

"There were found: 18 species of the genus *Aëdes,* 3 species of *Culex,* 2 species of *Anopheles* and 1 species of *Theobaldia* (Table I).

"The species of the genus *Aëdes* were caught in the largest quantities and they are found to be the most aggressive forms in relation to the man. They were found most frequently in the first part of the vegetative season. The species of the genus *Culex* was dominant in the final part of the season (Table II).

"Average intensity of the attacking gnats per hour amounted to 8–50 specimens. The maximal activity of gnats was stated to be in the morning hours."

CH'IN, Yao-Ting. [**Notes on some Species of Mosquitoes collected in the Northeastern Part of China with reference to Distributions**] *Acta Entomologica Sinica.* 1959, June, v. 9, No. 3, 281–7, 8 figs. [11 refs.] [In Chinese.]

The English summary appended to the paper is as follows:—

"1. A review of literature and examination of material in my collection

accumulated since 1936 showed that there are 33 species of mosquitoes present in the northeastern part of China. They are:

1. *Anopheles* (*A.*) *hyrcanus* var. *sinensis* Wiedemann, 1828;
2. *Anopheles maculipennis* Meigen, 1818;
3. *Anopheles* (*M.*) *pattoni* Christophers, 1926;
4. *Anopheles* (*A.*) *lindesayi* Giles, 1900;
5. *Theobaldia* (*Th.*) *kanayamensis* Yamada, 1932;
6. *Theobaldia* (*Th.*) *alaskaensis* Ludlow, 1906;
7. *Theobaldia* (*Cu.*) *ochroptera* Peus, 1935;
8. *Aëdes* (*O.*) *dorsalis* Meigen, 1832;
9. *Aëdes* (*A.*) *vexans* Meigen, 1830;
10. *Aëdes* (*F.*) *koreicus* Edwards, 1921;
11. *Aëdes* (*F.*) *seoulensis* Yamada, 1921;
12. *Aëdes* (*S.*) *chemulpoensis* Yamada, 1921;
13. *Aëdes* (*B.*) *lineatopenis* Ludlow;
14. *Aëdes* (*O.*) *maculatus* Meigen, 1804;
15. *Aëdes* (*S.*) *albopictus* Skuse, 1894;
16. *Aëdes* (*F.*) *niveus* Ludlow, 1903;
17. *Aëdes* (*F.*) *togoi* Theobald, 1907;
18. *Aëdes* (*O.*) *flavescens* Müller, 1764;
19. *Aëdes* (*O.*) *punctor* Kirby, 1837;
20. *Aëdes* (*O.*) *cataphylla* Dyar, 1916;
21. *Aëdes* (*O.*) *communis* Degeer, 1776;
22. *Aëdes* (*O.*) *pullatus* Coquillett, 1904;
23. *Aëdes* (*O.*) *excrucians* Walker, 1856;
24. *Culex* (*C.*) *pipiens* var. *pallens* Coquillett, 1898;
25. *Culex* (*C.*) *vagans* Wiedemann, 1828;
26. *Culex* (*C.*) *bitaeniorhynchus* Giles, 1901;
27. *Culex* (*C.*) *tritaeniorhynchus* Giles, 1901;
28. *Culex* (*B.*) *modestus* Ficalbi, 1890;
29. *Culex* (*N.*) *hayashii* Yamada, 1917;
30. *Culex* (*C.*) *orientalis* Edwards, 1921;
31. *Culex* (*C.*) *mimeticus* Noê, 1899;
32. *Culex* (*L.*) *vorax* Edwards, 1921;
33. *Culex* (*C.*) *vishnui* Theobald, 1901.

" 2. Of the 33 species *Culex* (*C.*) *vishnui* and *Theobaldia* (*Th.*) *kanayamensis* are new records for the northeastern provinces while *Aëdes* (*O.*) *communis, Aëdes* (*O.*) *punctor, Aëdes* (*O.*) *flavescens, Aëdes* (*O.*) *cataphylla, Aëdes* (*O.*) *pullatus, Aëdes* (*O.*) *excrucians, Theobaldia* (*Th.*) *alaskaensis* and *Theobaldia* (*Cu.*) *ochroptera* are new records for China.

" 3. In this paper *Aëdes flavescens, Aëdes punctor* and *Theobaldia alaskaensis* are described in detail; *Aëdes communis, Aëdes cataphylla, Aëdes* (*O.*) *pullatus, Aëdes* (*O.*) *excrucians* and *Theobaldia ochroptera* will be treated in a later paper.

" 4. The distribution of the Anopheline species is spotted in a map; the detail locations are:

a) *Anopheles maculipennis*: Kukenerh, Yakeshih, Yituliho, Hailar, Hake, Tsalantun, in the north-eastern part of Inner Mongolia, and in Peian, Heiho, Ohpu, in the western part of Heilungkiang Province.

b) *Anopheles lindesayi*: Suichung and Kienchang in Liaoning Province.

c) *Anopheles pattoni*: Dairen, Fuhsien, Chinchow, Hsingcheng, Suichung, Fuhsin, Yihsien in Liaoning Province.

d) *Anopheles hyrcanus* var. *sinensis*: Ubiquitous in all three provinces.

" 5. Mosquitoes caught in nature in which the virus of Encephalitis Japanese B Type has been isolated consisted of:

(1) *Culex pipiens* var. *pallens*, isolated in Shenyang and Dairen;

(2) *Culex tritaeniorhynchus* isolated in Dairen;

(3) *Aëdes vexans* isolated in Shenyang."

HARA, J. **Taxonomical Notes on the Female Terminalia of some Anopheline Mosquitoes of Japan and Formosa (With the Key to the Species and 13 Plates). Taxonomical and Ecological Studies on Mosquitoes of Japan. (Part 12.)** *Japanese J. Exper. Med.* 1959, Apr., v. 29, No. 2, 107–19.

SERVICE, M. W. **A New Species of the Genus *Aëdes* from Southern Nigeria.** *Proc. Roy. Entom. Soc. of London.* Ser. B. 1959, June 19, v. 28, Pts. 5/6, 73–6, 3 figs.

SAUTET, J., ALDIGHIERI, R., ALDIGHIERI, J. & VUILLET, F. Une nouvelle souche d'*Aedes aegypti* peu sensible au DDT, provenant de Saigon. [**A New Strain of** *Aëdes aegypti* **Weakly Sensitive to DDT, obtained from Saigon**] *Bull. Soc. Path. Exot.* 1959, Jan.–Feb., v. 52, No. 1, 34–6, 1 fig.

RACHOU, R. G., FERREIRA, M. O., MARTINS, C. M. & FERREIRA NETO, J. A. Variação mensal da densidade domiciliária do *Culex pipiens fatigans* em Florianópolis (Santa Catarina). [**Monthly Variation in the Density of** *Culex fatigans* **in Houses in Florianopolis, Santa Catarina, Brazil**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1958, Jan., v. 10, No. 1, 51–9, 4 graphs. English summary.

BRYGOO, E. R., DODIN, A. & SUREAU, P. Repas sanguin de *Culex fatigans* sur *Chamaeleo.* [**Blood Feeding of** *C. fatigans* **on Chameleons**] *Arch. Inst. Pasteur de Madagascar.* 1959, v. 27, 59–62.

————, SUREAU, P. & DODIN, A. Survie des *Culex fatigans* gorgés sur *Chamaeleo.* [**Survival of** *C. fatigans* **engorged on Chameleons**] *Ibid.*, 63–8, 3 figs.

DODIN, A. & BRYGOO, E. R. La thiamine n'empêche pas *Culex fatigans* de se nourrir sur *Chamaeleo.* [**Thiamine does not Prevent** *C. fatigans* **from Feeding on Chameleons**] *Ibid.*, 69–70.

WIRTH, W. W. & BLANTON, F. S. **Biting Midges of the Genus** *Culicoides* **from Panama (Diptera: Heleidae).** *Proc. U.S. Nat. Museum.* Wash. 1959, v. 109, No. 3415, 237–482, 91 figs. [Numerous refs.]

RIOUX, J. A., DESCOUS, S. & PECH, J. Un nouveau Cératopogonide arboricole: *Culicoides haranti* n. sp. (*Diptera, Heleidae*). [**A New Arboreal Ceratopogonid,** *Culicoides haranti*] *Ann. Parasit. Humaine et Comparée.* 1959, v. 34, No. 3, 432–8, 3 figs.

CLASTRIER, J. Notes sur les Cératopogonidés. VII. Cératopogonidés d'Afrique Occidentale Française (4). [**Notes on Ceratopogonids. VII. Ceratopogonids of French West Africa**] *Arch. Inst. Pasteur d'Algérie.* 1959, June, v. 37, No. 2, 240–83, 30 figs. [20 refs.]

ABONNENC, E. Étude comparative des femelles de *Phlebotomus papatasi* Scopoli, de *Phlebotomus papatasi* var. *bergeroti* Parrot et de *Phlebotomus duboscqi* Neveu-Lemaire. [**Comparative Studies of Females of** *Phlebotomus papatasi, Phlebotomus papatasi bergeroti* **and** *Phlebotomus duboscqi*] *Arch. Inst. Pasteur d'Algérie.* 1959, June, v. 37, No. 2, 329–39, 5 figs. [11 refs.]

BARRETO, M. P., MARTINS, A. V. & PELLEGRINO, J. Notas sôbre flebotomíneos do Nordeste do Estado de Minas Gerais, com as descrições de duas especies novas (Diptera, Psychodidae). [**Notes on *Phlebotomus* from the North East of Minas Gerais, Brazil, with a Description of Two New Species**] *Folia Clin. et Biol.* S. Paulo. 1956, July–Dec., v. 26, Nos. 1/6, 47–56, 14 figs. on 2 pls.

The English summary appended to the paper is as follows:—

"A collection of phlebotomes was made during the last days of October, 1955, in two localities of the Northeast of the State of Minas Gerais, Brazil.

"Eight already known species were found: *S. intermedia* (Lutz & Neiva), *S. migonei* (França), *S. cortelezzii* (Breth.), *S. fischeri* (Pinto), *S. tupynambai* (Mang.), *S. peresi* (Mang.), *S. minasensis* (Mang.), and *S. serrana* (Dam. & Arouck). Certain morphological differences observed in *migonei*, *cortelezzii*, *fischeri*, *tupynambai* and *serrana* are discussed.

"Finally two new species, *S. firmatoi* and *S. ferreirana*, from Jampruca, Minas Gerais, Brazil, are described."

WILSON-JONES, K., DAVIDSON, G. & HEWLETT, P. S. **Dosage-Mortality Curves for Houseflies susceptible and resistant to DDT.** [Correspondence.] *Nature.* 1958, Aug. 9, v. 182, 403–4, 2 figs.

In reply to a recent paper by HEWLETT [this *Bulletin*, 1958, v. 55, 832], an alternative explanation is offered for the fact that the slopes of dosage mortality curves for house-flies resistant to DDT are less steep than those for house-flies susceptible to DDT.

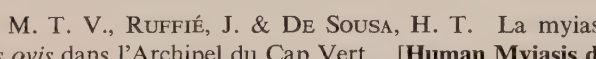
It is considered that the difference in the slopes of the two dosage-mortality curves is representative principally of the difference between pure and impure samples. While a resistant strain is made up of a number of different genotypes (the number depending on the mode of inheritance of resistance), a field collected susceptible colony will be much more homozygous; the occurrence of resistant genes in a population unselected by insecticide is very low.

Evidence for this theory is drawn from genetic studies with *Anopheles gambiae*. *R. J. Wood*

BRADBURY, F. R. & STANDEN, H. **Metabolism of Benzene Hexachloride by Resistant Houseflies** *Musca domestica.* [Correspondence.] *Nature.* 1959, Apr. 4, v. 183, 983–4.

It has been previously demonstrated [this *Bulletin*, 1957, v. 54, 266] that a resistant strain of house-flies rapidly metabolizes both the alpha and gamma isomers of benzene hexachloride to water-soluble metabolites, releasing chlorine ions. It has now been shown that, under alkaline hydrolysis, these metabolites (the nature of which is unknown) are converted into dichlorothiophenols. These were identified by the method of isotopic dilution but have not yet been isolated. Dichlorothiophenol amounts to approximately 68% of the water-soluble products from the alpha isomer and 61% from the gamma isomer. "It is inferred that the metabolism of benzene hexachloride by the flies to

produce water-soluble compounds involves the formation of a C–S bond." A theoretical scheme is given:



$$C_6H_6Cl_6 + HSR \rightarrow C_6H_6Cl_5.S.R \rightarrow C_6H_3Cl_2SH + ROH + 3HCl.$$

It is possible that HS*R* is reduced glutathione, essential for the benzene hexachloride process *in vitro*.

In vitro investigation demonstrated a conversion of alpha and gamma benzene hexachloride to water-soluble compounds which then yielded thiophenols on alkaline hydrolysis. "The *in vitro* reaction did not proceed in the absence of added glutathione." *R. J. Wood*

ELDEFRAWI, M. E., MISKUS, R. & HOSKINS, W. M. **Resistance to Sevin by DDT- and Parathion-Resistant Houseflies and Sesoxane as Sevin Synergist.** *Science*. 1959, Apr. 3, v. 129, 898–9, 1 fig.

The following is virtually the authors' summary:—

The new carbamate insecticide, 1-Naphthyl N-methyl carbamate (Sevin), has a low toxicity against house-flies. However, it is activated effectively by low concentrations of 2-(3,4-methylenedioxyphenoxy)-3,6,9-trioxaudecane (Sesoxane), a pyrethrin synergist. This occurs with normal non-selected flies and also with strains selected for resistance to DDT and parathion, which have considerable cross-resistance to Sevin. *E. R. Nye*

DE MEIRA, M. T. V., RUFFIÉ, J. & DE SOUSA, H. T. La myiase humaine à *Oestrus ovis* dans l'Archipel du Cap Vert. [**Human Myiasis due to** *Oestrus ovis* **in the Cape Verde Islands**] *Anais Inst. Med. Trop.* Lisbon. 1957, Sept.–Dec., v. 14, Nos. 3–4, 407–23, 4 figs. on 2 pls.

DE MEIRA, M. T. V., RUFFIÉ, J. & DE SOUSA, H. T. Algumas carraças de ilhas de Cabo Verde. [**Some Ticks of the Cape Verde Islands**] *Anais Inst. Med. Trop.* Lisbon. 1957, Sept.–Dec., v. 14, Nos. 3/4, 425–7.

The English summary appended to the paper is as follows:—

"The authors found in some of Cape Verd islands species of ticks as follows: *Amblyomma variegatum* (Fabricius, 1749) and *Margaropus decoloratus* (Koch, 1844), in oxen; one nymph of *Hyalomma* sp. (Koch, 1844), in a bird of prey; 4 nymphs of *Rhipicephalus sanguineus* (Latreille, 1804), free in the grass. In other species of birds ticks were not found.

"*Amblyomma variegatum*, which is very frequent in Cape Verd, had been found by Meira *et al.* in the Boa Vista island 1946, and by Tendeiro, in the Santiago Iso, 1950."

HOOGSTRAAL, H. **On** *Allophysalis*, **a New Subgenus of** *Haemaphysalis* **(Ixodoidea, Ixodidae).** *J. Egyptian Pub. Health Ass.* 1959, v. 34, No. 1, 37–42.

TAUFFLIEB, R. & MOUCHET, J. Notes sur les acariens (*Acarina*: *Laelaptidae* et *Spinturnicidae*) du Cameroun. [**Notes on Acarines of the Cameroons**] *Ann. Parasit. Humaine et Comparée.* 1959, v. 34, No. 3, 350–53. [12 refs.]

VERANO, O. T. & GALVÃO, A. B. *Triatoma costalimai* sp. n. [*Triatoma costalimai,* **n. sp.**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1958, Apr., v. 10, No. 2, 199–205, 4 figs. English summary (7 lines).

CLARKE, T. H. & COCHRAN, D. G. **Cross-Resistance in Insecticide-Resistant Strains of the German Cockroach,** *Blattella germanica* **(L.).** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 5, 823–33, 8 figs. [19 refs.]

" The authors describe a series of experiments designed to determine the extent to which cross-resistance exists in insecticide-resistant strains of the German cockroach. The tests were conducted by exposing females from a DDT-resistant strain, a chlordane-resistant strain, and a non-resistant strain to varying concentrations of several insecticides. From these tests mortality data were obtained and are presented in the form of regression lines.

" The insecticides used were DDT, methoxychlor, chlordane, dieldrin, Prolan, malathion, allethrin, and Lethane ; these were chosen so that a wide variety of chemical types would be represented.

" The results indicate that the DDT-resistant strain is highly resistant to DDT and to its analogue, methoxychlor, but not to any of the other insecticides tested. Similarly, the chlordane-resistant strain is highly resistant to chlordane and to its analogue, dieldrin, but is susceptible to the other toxicants listed.

" From these results, as well as those obtained by others, it appears that the picture of cross-resistance in the German cockroach is in essential agreement with that which is emerging for other insects throughout the world."

GEROLT, P. **'Vapour Toxicity' of Solid Insecticides.** [Correspondence.] *Nature.* 1959, Apr. 18, v. 183, 1121–2.

Mathematical and experimental evidence is given in criticism of the standard procedure for testing the toxic properties of vapours from crystalline deposits of DDT and gamma BHC. It has been usual to assess the " vapour toxicity " of an insecticide by exposing test insects in cages held a short distance from treated surfaces. But this method is now considered unsatisfactory and liable to give results of highly questionable value. The toxic effect often observed in such experiments is " mainly caused by insecticide acquired . . . in an indirect way, namely, via a condensed film formed on the body of the holding cage ". No mortality was observed in *Drosophila melanogaster* and *Aëdes ægypti* exposed to *unsaturated* vapour for 24 hours.

Estimates were made of the actual amounts of insecticide condensed on a glass surface overnight in a closed system. Condensates of gamma BHC were sufficient to kill 20 female house-flies in 24 hours. With more susceptible

insects, such as *D. melanogaster* and *Aëdes aegypti,* complete mortality was also obtained with DDT.

It is concluded that, where the literature refers to the " vapour effect " of an insecticide, it in fact refers to " surface deposits of condensed vapour plus the effect of an eventual condensate directly on the insect ". *R. J. Wood*

LONERGAN, R. P. & HALL, L. B. **The Regulation of Flow through Residual Spray Nozzles. 1. Metering Orifices in Polyethylene Discs.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 5, 955–9, 2 figs. **2. Flow Control Orifices in Soft Rubber Discs.** *Ibid.,* 961–71, 7 figs.

i. " Used residual spray nozzles, which have been discarded because of the increase in discharge rates, may be used again if their discharge rates are reduced by a metering orifice placed in the nozzle tip. A suitable orifice in a polyethylene disc is described. On the basis of laboratory test results, such a disc appears to be an inexpensive and satisfactory metering device for use in combination with worn spray nozzles."

ii. " A sharp-edged orifice in a disc of rubber with a durometer tolerance of 35 to 40, properly mounted near the nozzle tip, is capable of regulating the discharge from a compression sprayer with an accuracy at least comparable to that of mechanical pressure regulator valves. The orifice can act as a flow control device under varying hydraulic pressures because of reduction of the diameter and change of the shape of the orifice under the fluid pressure on the upstream face of the disc. This is possible since, to maintain a constant rate of discharge, the diameter of the orifice need only be changed inversely as the fourth root of the pressure and the square root of the coefficient of discharge. Erosion of the orifice and ' set ' of the rubber, two potential causes of inaccurate flow, tend to cancel each other out.

" The device is best used in combination with an 8003 nozzle tip. The rubber discs can be produced commercially at a reasonable cost. Field trials of the combination are recommended."

PAULINI, E., MEMÓRIA, J. M. P., DE PAULA, O. R. & SOBRINHO, J. M. A. Estudo relativo a fatôres ligados ao inseticida e à sua aplicação que influem sôbre a eficácia da desinsetização domiciliária: II. Experiências sôbre a distribuição do liquído no leque de bicos aspersores. [**Factors Relating to Insecticides and their Application which Influence House Spraying. II. Studies of the Distribution Pattern and Spray Angle of Spray Nozzles**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1958, Jan., v. 10, No. 1, 31–7. English summary (8 lines).

See this *Bulletin*, 1957, v. 54 (1374).

INGLES, L. G. Notas acerca de los mamíferos mexicanos. [**Observations on Mexican Mammals**] *An. Inst. Biol.* Mexico. 1958, v. 29, Nos. 1/2, 379–408.

DEVERS, R., RUZETTE, M. A. & SALVI, S. Une campagne de contrôle des gerbilles, *Tatera valida* Bocage, à la plaine de la Ndjili, Léopoldville. **[Control of Gerbils, *Tatera valida*, on the Ndjili Plain, Léopoldville]** *Ann. Soc. Belge de Mèd. Trop.* 1959, Apr. 30, v. 39, No. 2, 145–66, 1 plan, 1 graph & 11 figs. on 4 pls. [10 refs.]

LABORATORY PROCEDURES

BRUCE-CHWATT, L. J. **Anisol—a Convenient Immersion Medium for Microscopy.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 1, 151–3. [Refs. in footnotes.]

This useful little paper reviews the use of immersion media used in microscopy, with particular reference to malaria parasites in blood films. Cedar wood oil and other media have certain disadvantages and may be conveniently replaced by either methyl benzoate (oil of Niobe) or methyl phenyl ether (anisol). The latter is not greasy or sticky, completely volatilizes in half an hour, and does not affect Romanowsky staining. Its only real disadvantage is its fluidity. Ordinary immersion oil containers are often awkward to handle; a convenient substitute is the flat, plastic oilcan from which an exact amount of oil may be squeezed as required. *P. C. C. Garnham*

MISCELLANEOUS PAPERS

DAVIES, J. N. P. **The Development of 'Scientific' Medicine in the African Kingdom of Bunyoro-Kitara.** *Med. History.* Farnham. 1959, Jan., v. 3, No. 1, 47–57, 3 figs. on 2 pls. [17 refs.]

In this paper Davies gives some account of the kingdom of Bunyoro-Kitara, Uganda, and goes on to describe the kind of primitive surgical operations—ritual mutilations, trephinings and amputations—commonly carried out by primitive peoples. He then recalls the account given by Felkin, a missionary who had had 2 years of medical study, of a caesarean section performed in his presence by an African in 1879 at a time when this operation was regarded in England as one of the greatest gravity, and when aseptic surgery had not yet been born.

The African and his assistants performed the operation on a healthy woman half intoxicated with banana wine and tied to a bed; the incision through the abdominal wall and the uterine wall was swift and confident. The child was delivered, the uterus emptied and squeezed until it contracted, and the wound

edges (but not the uterine edges) were held together and secured by skin tied over polished iron spikes inserted for the purpose. The whole procedure was carried out with smooth and practised efficiency. Felkin observed the patient for 6 days, during which progress was very good.

Davies discusses the credibility of this account and concludes that there is nothing in it or in Felkin's other writings to suggest that it is not true. The knife was given to Felkin and is now in the Wellcome Historical Medical Museum.

Other accounts show that the Bunyoro people deliberately inoculated infants with syphilis to prevent them from getting the disease later, and there is an old history of deliberate investigation to find a cure for sleeping sickness; these, together with the present story of caesarean section suggest "an attitude to disease quite extraordinary in a preliterate people". It is evident that both magical and purely rational medical procedures were carried out at the same time, and the history of this rational medicine, unfortunately now lost, would probably have revealed that it was far more widespread than we tend to think in this remarkable people, who must have developed their attitude unaided from outside. *Charles Wilcocks*

WILD, H. & GELFAND, M. **Some Native Herbal Remedies at present in Use in Mashonaland.** *Central African J. of Med.* 1959, June, v. 5, No. 6, 292–305.

The structure of pharmacologically active plant constituents has often shown the synthetic chemist where to look for new drugs. There has been a revival of interest in traditional herbal remedies; one of the chief difficulties has been the accurate identification of the botanical source of the drug.

This paper describes a useful survey carried out in the Mashonaland area of Rhodesia by a botanist, a physician and a reliable interpreter, together with 5 independent local medicine men who had been persuaded to cooperate. Tables show the vernacular name of each drug, its botanical source, method of preparation and reputed value. The survey covers 240 specimens and includes 143 botanical species.

The authors point out that the majority of the medicines owe their reputation to the mediaeval principle of signatures, psychological effects, and the natural disappearance of symptoms. However, some of the remedies are used widely and the plants from which they are derived are likely to contain active substances.

The authors suggest that *Heeria reticulata, Dicoma anomala, Ochna pulchra* and *Elephantorrhiza goetzei* (for abdominal pain or diarrhoea), *Cassia abbreviata* (for gonorrhoea), *Securidaca longepedunculata* (for backache), *Lasiosiphon kraüssianus* (for anorexia; also a fish poison and a reputed abortifacient) and *Schwartzia madagascariensis* (for convulsions, sterility and swellings) would be worthy of further study. *L. G. Goodwin*

BOOK REVIEWS

FIESE, Marshall J. [M.D., F.A.C.P.] **Coccidioidomycosis.** With a foreword by Charles E. SMITH, M.D. pp. xiii + 253, frontispiece & 32 figs. 1958. Springfield: Charles C. Thomas, 301–327, East Lawrence Avenue, Ill., U.S.A. Toronto: Ryerson Press. Oxford: Blackwell Scientific Publications, Ltd. [72s.]

This comprehensive monograph on coccidioidomycosis is written by one who is evidently a master as well as a devotee of his subject. A native of the endemic area in which the disease occurs, namely, the San Joaquin Valley of California, he was naturally predisposed to undertake this task.

The foreword is written by Dr. Charles Smith, himself perhaps the greatest living authority on coccidioidomycosis. Of Dr. Fiese he says: "he has seen and viewed . . . countless roentgenograms, seen and studied the tragic autopsies, and perhaps most importantly of all, lived for years in the coccidioidal countryside".

An exceptionally clear literary style and an enthusiasm which can derive only from first-hand experience of the disease have combined to produce this fascinating, stimulating and richly informative account of coccidioidomycosis. The 14 chapters which comprise it include, with many subsections: the history of research on coccidioidomycosis, its geographical distribution and epidemiology, its mycology and pathology, its clinical features and treatment and, in addition, a chapter on coccidioidomycosis in animals. Of particular interest are the sections on serological procedures and their significance and relative value in the diagnosis of the clinical varieties of the disease, the description of the radiographic findings, and lastly, the assessment of the value of some of the more promising of a long list of drugs which have been tried out in attempts to cure this disease.

A very comprehensive bibliography is appended and testifies to the wide scope of this book. Also included are a number of high quality illustrations and tables. The type, which is easy to read, is printed on glossy art paper.

C. J. La Touche

HAFFKINE INSTITUTE. **Diamond Jubilee, 1899–1958. Souvenir.** pp. viii + 140, illustrated. 1959. Bombay 12; Parel, India.

This is a souvenir volume to commemorate the 60th anniversary of the foundation of this famous institute, which was started in 1899 as the plague research laboratory at a time when plague was raging, and which was renamed after Haffkine in 1925.

The volume contains articles prepared specially for it, and the first 9 of these are general in interest. The first, by the present Director of the institute, H. I. JHALA, is a brief history of the institute and of Haffkine's work there. The others are summaries of recent work—for instance the paper on the passing of plague by S. S. SOKHEY, on rabies by R. S. RAO, on diet and liver injuries by M. V. R. RAO and S. M. PATEL, on serological studies in plague by S. C. SEAL, on human haemoglobin by J. B. CHATTERJEA—or are essays on chosen subjects—for instance on biological standardization by B. MUKERJI, on Indian indigenous drugs by I. C. CHOPRA, K. L. HANDA and R. N. CHOPRA, and on good laboratory animals by W. LANE-PETTER.

The second part of the book contains 8 papers by different authors on the work done by the various departments from their inception to the present time. These papers are quite short but informative. They are illustrated by photographs, and they certainly give a reader a lucid account of important research work. The institute now contains departments of vaccine, of clinical pathology and diagnostic reagents, of virus diseases (including rabies), of pharmacology, of biochemistry, of entomology, of chemotherapy, and of antitoxins and sera. The institute undertakes field investigations such as the investigation of outbreaks of scrub typhus, or epidemic dropsy, or field surveys of mosquitoes, besides the more recondite researches into clinical and immunological problems.

At the end there is a list of 436 contributions to the literature made by members of the staff since 1897 (when Haffkine first announced his vaccine and tried it on himself). These are set out in chronological order.

The book contains a coloured portrait of Haffkine, and a page of photographs of past directors and the present director. Haffkine himself was of Russian origin, 4 Directors were British and 4 (from 1932 onwards) were Indian. Those who work in the institute must feel a sense of continuity and style, and this volume will be a memorable factor in preserving and heightening it.

Charles Wilcocks

BRUMPT, E. & NEVEU-LEMAIRE, M. **Travaux pratiques de parasitologie.** [Practical Parasitology] 6th Edition revised and completed by Lucien BRUMPT. pp. vi + 317. 203 figs. 1958. Paris (VIe): Masson et Cie., 120, Boulevard St.-Germain.

Textbooks which have run into six editions have a tendency to become corpulent in form and prosy in outlook. Not so this small volume, which, although in its thirty-first year, shows no sign of middle-aged spread and is as alert and vigorous in style as when it first appeared.

In the introduction to the present edition [wrongly referred to in the table of contents as the fifth] the authors state that each succeeding edition has been revised and brought up-to-date. At first glance it is difficult to understand how this has been so successfully accomplished with so little increase in the length of the text (the first edition contained some 300 pages, the sixth 316). The obvious explanation is that the authors have rigidly adhered to their original intention of supplying a guide or elementary introduction to an extensive and complicated subject, the essential facts of which had at the time when their book was first published, already been firmly established. It is for this reason that substantial additions to the later editions are, with a few notable exceptions, comparatively few; among such additions are those dealing with the viral, rickettsial and spirochaetal infections, toxoplasmosis, the exo-erythrocytic cycle in malaria, and the life cycles and transmission of the non-periodic filarial worms. There are, of course, many minor additions concerning our knowledge of parasites and their vectors, together with many modifications of the views expressed in previous editions, these modifications sometimes being in the form of confirmation of earlier conjectures—indeed it is remarkable how often "it is probable that" in the earlier editions has become "it has been proved that" in the present edition. Among omissions, one notes that no account is given in the entomological section of the genus *Culicoides*, a failure to which attention was drawn in the review of the first edition [this

Bulletin, 1929, v. 26, 434], and that no reference is made to the use of methylene-blue azure (" Field's stain ") for the recognition of the malaria parasite in thick films.

This last edition of " Brumpt and Neveu-Lemaire " can, like its predecessors, be recommended to all interested persons as a concise and up-to-date account of the morphology and mode of life of the more common parasites occurring on and in the human host. *R. M. Gordon*

CALLOT, Jacques & HELLUY, Joseph. **Parasitologie médicale.** [Medical Parasitology] pp. 645 + xxix in loose leaf binder, 263 figs. & 6 coloured pls. 1958. Paris-VIe: Éditions Médicales Flammarion, 22, rue de Vaugirard.

This book is in the loose leaf form, familiar to students of tropical medicine from VAUCEL's textbook, which is published also in this edition and from which the 6 coloured plates of malaria parasites are taken. In a growing subject this type of production is useful because new material is easily inserted at yearly intervals. The authors deal with the subject of parasitology with a remarkable brevity and omission of much detail; for this reason also it should be easy to keep the work up to date. Although the authors have tried to treat the subject from the biological angle and to restrict morphological and systematic details to a minimum, in fact they have been driven—by the nature of the science—to include the major characters of each organism. These are well illustrated in 263 line drawings, with scales, including useful designs of the internal anatomy of arthropods.

A short introduction is devoted to the principles of human parasitology. The work is then divided into five books, dealing respectively with the arthropods, helminths, protozoa, fungi, and technique. The bacteria, rickettsiae, spirochaetes and viruses are considered under the arthropods in nearly a hundred pages, and it seems illogical to place them in this secondary place; the arthropods are described almost entirely as vectors of pathogens, and if this group is to claim predominant place, why should not snails be treated similarly? The mixed nature of the subject, however, inevitably entails difficulty in presentation.

Each infection is described under the following heads: the morphology and biology of the organism; epidemiology, including geographical distribution, animal reservoirs, and modes of transmission; clinical features; diagnosis; treatment; control. The book is thus almost a synopsis and will prove invaluable for quick reference.

A book of this range can hardly be free of errors or minor defects, and examples of these are the poor illustrations of leptomonads (in Fig. 184), actual mistakes such as the statement that *Eimeria stiedai* [*sic*] is exceptionally a human parasite, and the citation in the bibliography of unpublished theses as major references. *P. C. C. Garnham*

GHERMAN, I. **Elemente de epidemiologie a bolilor parazitare.** [Elements of Epidemiology of Parasitic Diseases] 176 pp. 58 pls. 1958. Bucharest: Editura Medicală. [Lei 28.]

The author has endeavoured to give a succinct account of the principles of the epidemiology of the parasitic diseases of man encountered in Rumania,

together with the more important ones found in other countries, and has produced a book designed for the instruction of medical students, epidemiologists and parasitologists. There are 131 pages of text divided into sections, devoted to descriptions of diseases caused by protozoa, cestodes, trematodes, nematodes and a chapter on filariae. The account of each disease covers the aetiology with a description of the morphology of the causative organism, the epidemiology, with an account of the natural reservoir of infection and means of transmission of the disease to man, and the measures of prophylaxis. The text is followed by 20 pages of synoptic tables in which the preceding information is conveniently summarized. Treatment is not dealt with except for a brief appendix on the dosages employed in the treatment of patients suffering from malaria. There is a biblography of 195 references, including a fair proportion of works by Rumanian authors. The book is concluded with a section consisting of 58 instructive synoptic charts, which illustrate the aetiology and natural history of the diseases under consideration. *D. J. Bauer*

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